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BY
STEFFAN WITTRUP CHRISTENSEN

DISSERTATION SUBMITTED 2017

AALBORG UNIVERSITY
DENMARK

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by

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Dissertation submitted

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In 2005, Steffan received a Bachelor in physiotherapy from VIA University College, Holstebro, Denmark, and in 2009 he was awarded a Master's in musculoskeletal physiotherapy from the University of Queensland, Australia. Since his authorisation as a physiotherapist in 2005, he has worked clinically with musculoskeletal disorders. His clinical work with patients who often suffered from complex painful conditions, lead him towards this PhD with the aim of understanding the effect of neck pain on pain sensitivity and muscle function.

PREFACE

This purpose of this PhD is to investigate the link between neck pain and shoulder movements with regard to sensory and motor aspects of both acute experimental neck pain in healthy participants, as well as ongoing neck pain in a clinical population. The thesis is based on three peer-reviewed articles, which will be referred to as I-III. The articles are based on three individual experimental studies, which were carried out from 2012-2015 at the Center for Sensory Motor Interaction, Aalborg University, Denmark.

Study I
SW Christensen, RP Hirata & T Graven-Nielsen. 2015. The effect of experimental neck pain on pressure pain sensitivity and axioscapular motor control. *J Pain,* 16**,** 367-79

Study II
SW Christensen, RP Hirata & T Graven-Nielsen. 2017. Bilateral experimental neck pain reorganize axioscapular muscle coordination and pain sensitivity. *Eur J Pain,* 21**,** 681-691

Study III
SW Christensen, RP Hirata & T Graven-Nielsen. Altered pain sensitivity and reorganized axioscapular muscle coordination is a feature of ongoing neck pain. (Submitted).

ENGLISH SUMMARY

Neck pain is a significant problem with yearly costs estimated to exceed DKK 2.9 billion in Denmark alone. With the scale of this problem, there is a need for a better understanding of the underlying mechanisms behind clinical findings such as increased pain sensitivity and reorganized muscle activity. One of the areas that has been proposed as a potential contributing factor to neck pain, is the shoulder girdle, due to its close anatomical link to the cervical spine. The assertion that the shoulder girdle might play a role in neck pain is supported by reports from neck pain patients describing their symptoms being aggravated following upper limb activity, as well as studies showing reorganized muscle activity of the axioscapular muscles in ongoing neck pain conditions when compared to a pain-free population. However, previous studies conducted in this area have been criticised for using different methods and neck pain populations, thereby making it hard to compare results between studies.

The current work set out to explore the relationship between neck pain, pain sensitivity and axioscapular motor control during acute and ongoing neck pain. In order to investigate this, three studies were conducted using a standardized setup, where participants performed repeated series of arm movements. To examine the effect of acute neck pain, an experimental model of neck pain was used in healthy participants. This involved injections of hypertonic saline, to induce muscle pain in a neck muscle not functionally connected to the shoulder, either unilaterally (Study I) or bilaterally (Study II). Such a model of experimental neck pain allows for investigation of the effects of pain immediately after onset, and it may mimic some features of what might be present following the initial onset of clinical neck pain. To investigate the effect of ongoing neck pain two patient populations, insidious onset of neck pain (IONP) and whiplash associated disorders (WAD), were recruited, along with a healthy control group (Study III). To quantify the painful experience, participants in all three studies were asked to rate the level of their pain on a visual analogue scale (VAS), indicate the area of pain on a body chart, and choose words from the McGill pain questionnaire that described their experienced pain. Pain sensitivity was determined by recordings of pressure pain threshold (PPT) before, in-between and after repeated series of arm movements. In order to determine muscle activity during the series of arm movements, electromyographic recordings were made from both axioscapular and trunk muscles.

Similar traits regarding pain intensity and area of pain were observed for both healthy participants during experimental neck pain (Study I&II) and patients with ongoing clinical neck pain (Study III). However, the clinical population (Study III) reported more words describing affective aspects of pain than what was reported by healthy participants experiencing experimental neck pain (Study I&II). In regard to PPT recordings, in healthy participants these were increased in distant areas following the experimental neck pain condition with bilateral pain (Study II), but not unilateral pain

(Study I), which contrasts the decreased PPT recordings in clinical neck pain (Study III). Not only did the two groups with ongoing clinical neck pain display widespread decreased PPTs compared to a healthy control group at baseline, this also got progressively worse with repeated series of arm movements. However, this was only significantly for the IONP group while the opposite, reduced pain sensitivity, was observed for healthy controls (Study III). In the current work, a clear link between acute experimental neck pain and altered function of the axioscapular muscles during arm movements was observed. The most consistent finding was reduced activity of the ipsilateral upper trapezius muscle (Study I&II). Additionally, for the first time, a direct link has been made between neck pain and altered trunk muscle activity, where bilateral neck pain caused bilateral increased muscle activity for the erector spinae muscles (Study II). These findings indicate that such changes might occur immediately after the onset of neck pain. For clinical neck pain, increased activity was observed for the serratus anterior muscle in the WAD group as rest periods between movement series was reduced, indicating that it might be a fatigue response (Study III).

The findings of the current work have shown that a relationship between neck pain, pain sensitivity, and axioscapular and trunk muscle activity exists. It has been demonstrated that such changes might occur immediately after the initial onset of experimental neck pain, though adaptations to pain might change during the transition from an acute onset of pain to an ongoing painful condition. Taken together, the findings of these three studies may be of great clinical importance, as they underline the importance of including both the shoulder girdle and the trunk, as well as pain sensitivity, when assessing and treating people suffering from neck pain. Furthermore, the results could imply that although two seemingly similar neck pain populations are performing the same standardized task, they do not respond the same way. This could indicate that clinicians should tailor their assessment and treatment to the individual neck pain patient rather than applying a standardized strategy solely based on the perceived area of pain.

DANSK RESUME

Nakkesmerter er et stort problem med årlige omkostninger, der i alene i Danmark er estimeret til at være mere end 2.9 billioner DKK. Med størrelsen af problemet er der et behov for en bedre forståelse af de underliggende mekanismer bag kliniske fund, så som ændret smertesensitivitet og reorganiseret muskel aktivitet. Et af de områder der er foreslået som en bidragende faktor til nakkesmerter er skulderen, grundet de tætte anatomiske forbindelser til nakken. At skulderen kan spille en rolle ved nakkesmerter, støttes af at mange personer med nakkesmerter rapporterer symptomforværring i forbindelse med aktiviteter, hvor overekstremiteterne bruges. Ligeledes viser studier reorganiseret aktivitet af de axioscapulære muskler, hos personer med vedvarende nakkesmerter, når disse sammenlignes med personer uden smerter. De studier der er lavet på området, er blevet kritiseret for at bruge forskellige metoder og population med nakkesmerter, hvilket gør det svært at sammenligne resultaterne mellem studierne.

Dette projekt har haft til formål at undersøge forholdene mellem nakkesmerter, smertesensitivitet og axioscapulær motorisk kontrol under akutte og vedvarende nakkesmerter. For at kunne undersøge dette, blev der gennemført tre studier med en standardiseret metode, hvor deltagerne udførte gentagne serier af armbevægelser. For at undersøge effekten af akutte nakkesmerter, blev der anvendt en eksperimentel smertemodel på deltagere uden smerter, hvor der blev indsprøjtet saltvand i en nakkemuskel, der ikke er funktionelt forbundet med skulderen. Smerten blev induceret, enten på den ene side (Studie I) eller på begge sider (Studie II) af nakken. En sådan smertemodel muliggør, at man kan undersøge effekten af smerte, umiddelbart efter den er induceret og den kan måske efterligne nogle af de elementer der indledningsvis kan være tilstede ved kliniske nakkesmerter. For at undersøge effekten af vedvarende nakkesmerter, blev der rekrutteret to grupper med kliniske nakkesmerter; En gruppe med ikke specifikke nakkesmerter (IONP) og en med følgesymptomer efter piskesmæld (WAD) samt en rask kontrolgruppe (Studie III). Til kvantificering af den smertefulde oplevelse hos deltagerne, blev de i alle tre studier bedt om at score intensiteten af deres smerter på en visuel analog skala (VAS); indikere området med oplevet smerte på et kropsskema samt vælge ord der beskriver den oplevede smerte fra et McGill smerte spørgeskema. Smertesensitivitet blev fundet ved at måle tryksmertetærsklen (PPT) før, imellem og efter de gentagne serier af armbevægelser. Til at måle muskelaktivitet under serierne af armbevægelser, blev der anvendt elektromyografiske optagelser fra både axioscapulære og truncus muskler.

For smerteintensitet og området af den oplevede smerte, blev der fundet sammenlignelige træk for både raske deltagere under den eksperimentelle smerte (Studie I&II) og grupperne med vedvarende nakkesmerter (Studie III). Kigger man i stedet på ordene, der blev brugt til at beskrive de oplevede smerter, brugte deltagerne

med kliniske nakkesmerter (Studie III) flere ord, der beskriver en emotionel dimension af smerte, end det der blev rapporteret af raske deltagere under eksperimentel smerte (Studie I&II). For PPT målingerne hos raske deltagere blev disse fundet øget, i områder væk fra smerten under de bilaterale (Studie II), men ikke unilaterale (Studie I) eksperimentelle nakkesmerter, hvilket står i kontrast til de reducerede PPT målinger hos personer med kliniske nakkesmerter (Studie III). Ikke alene viste de to grupper med vedvarende nakkesmerter udbredte reducerede PPT målinger, sammenlignet med den raske kontrolgruppe, de blev også gradvist værre under de gentagne serier af armbevægelser. Denne forværring var dog kun signifikant for IONP gruppen mens det modsatte, en mindsket smertesensitivitet, blev observeret for den raske kontrolgruppe (Studie III). I dette projekt er der blevet vist en klar sammenhæng, mellem akutte nakkesmerter og en ændret funktion af de axioscapulære muskler under armbevægelser. Det mest konstante fund var en reduceret aktivitet af den øvre trapezius muskle (Studie I&II). Ydermere, har dette projekt for første gang vist en sammenhæng mellem nakkesmerter og ændret aktivitet af truncus muskler, hvor bilaterale nakkesmerter forårsagede en øget bilateral aktivitet af erector spinae musklen (Studie II). Disse fund indikerer, at sådanne forandringer kan være til stede indledningsvis, efter man har fået ondt i nakken. For kliniske nakkesmerter blev der observeret en øget aktivitet for serratus anterior musklen hos WAD gruppen, når pauserne mellem serier af armbevægelser blev afkortet, hvilket kan indikere et udtrætningsrespons (Studie III).

Resultaterne fra dette projekt viser, at der er eksisterer en sammenhæng mellem nakkesmerter, smertesensitivitet og aktivitet af axioscapulære og truncus muskler. Det er blevet vist, at ændringer af disse måske sker allerede indledningsvis efter man har fået nakkesmerter, selv om adaptationerne til smerter måske ændres over tiden fra det akutte til den vedvarende smerte. Sammenlagt kan disse fund have stor betydning for klinisk praksis, da de understreger vigtigheden af at inkludere både skulderen og truncus, såvel som smertesensitivitet i både undersøgelse og behandling af personer med nakkesmerter. Ligeledes kan resultaterne indikere, at selv om to næsten identiske grupper med nakkesmerter udfører den samme standardiserede opgave, så responderer de ikke ens. Dette kan indikere, at klinikere skal skræddersy deres undersøgelse og behandling til den individuelle patient med nakkesmerter, frem for en standardiseret tilgang baseret på området hvor de oplever smerten fra.

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ABBREVIATIONS & ACRONYMS

AM Axioscapular muscles

EMG Electromyography

Hyperalgesia/hypoalgesia follows the IASP (International Association for the Study of Pain) taxonomy where hyperalgesia is described as an *increased response* to a stimulus while the opposite, a *raised threshold* and thereby a *decreased response* is used to describe hypoalgesia.

IONP Insidious onset of neck pain (also described as mechanical neck pain in the literature): Describes neck pain where no specific event, trauma or disease caused the onset.

NRS Numeric rating scale

Ongoing neck pain describes neck pain with daily symptoms for longer than 3 months. The term *ongoing* is chosen instead of *chronic* as it better describes a condition where symptoms may fluctuate in intensity within or between days.

PPT Pressure pain threshold follows the IASP taxonomy for pain threshold which defines it as *the minimum intensity of a stimulus that is perceived as painful.*

RMS Root mean square

Scaption describes abduction of the shoulder/arm in the scapular plane

VAS Visual analogue scale

WAD Whiplash Associated Disorder describes a number of symptoms caused by rapid acceleration/deceleration of the cervical spine, usually as a result of a motor vehicle accident (MVA)

TABLE OF CONTENTS

CHAPTER 1. INTRODUCTION

Painful musculoskeletal conditions are one of the most common causes of contact with the healthcare system (Mody and Brooks, 2012), and spinal pain is, without comparison, the most disabling musculoskeletal disorder in regard to years lived with disability (Vos et al., 2012). The sheer quantity of spine-related musculoskeletal conditions may explain why healthcare costs in this area are unrivalled by any other musculoskeletal condition (Haldeman et al., 2012). Most people will experience neck pain during their lifetime (Manchikanti et al., 2009) and many of these will develop ongoing neck pain (Borghouts et al., 1998, Bogduk, 2011). Given that it is a major cause of disability (Hoy et al., 2014), and compensation costs are rising (Côté, 2003), neck pain has become a focus for researchers and clinicians alike.

1.1. NECK PAIN – THE EXTENT OF THE PROBLEM

Reviews looking at studies from around the world have found a one month prevalence of neck pain ranging from 15.4% up to 45.3% (Hogg-Johnson et al., 2008, Fejer et al., 2006), with many developing ongoing neck pain after the initial onset (Borghouts et al., 1998, Bogduk, 2011). A recent report from the Danish Ministry of Health estimated that, during 2013, more than 50% of the general population had pain or discomfort from the neck or shoulder area within a 14 day period (Christensen et al., 2014). The large number of people suffering from neck pain in Denmark is reflected in the number of days of sick leave, of which neck pain accounts for 16%, along with 6% of all visits to a general practitioner, and 23% of all visits to chiropractors or physiotherapists (Flachs et al., 2015). When accounting for the large number affected, days of sick leave, treatments costs, and loss of productivity, the costs in Denmark alone are estimated to be more than DKK 2.9 billion per year (Flachs et al., 2015).

1.2. DEFINING NECK PAIN

The definition of neck pain varies throughout the literature. Neck pain has been defined based on the area, cause, severity or duration of pain, as well as the setting in which neck pain is experienced (Misailidou et al., 2010, Guzman et al., 2008), either separately or in combination. One of the commonly used definitions of neck pain has been proposed by the International Association for the Study of Pain (IASP) and is based on the anatomical location of neck pain: "*Pain perceived as arising from anywhere within the region bounded superiorly by the superior nuchal line, inferiorly by an imaginary transverse line through the tip of the first thoracic spinous process, and laterally by sagittal planes tangential to the lateral borders of the neck*" (Merskey et al., 1994). One big advantage of this definition is that it can be applied to neck pain of both insidious and traumatic onset, as it does not indicate the cause of pain but only where it is perceived (Bogduk, 2011).

1.3. NECK PAIN – UNDERSTANDING THE PROBLEM

For years, great efforts have been put into identifying the source of neck pain. Despite this, it is still often not possible to determine a pathoanatomical cause (Bogduk, 2011, Ferrari and Russell, 2003, Curatolo et al., 2011). Although the cause of neck pain remains elusive, considerable advances have been made in the knowledge on the topic. In this regard, links between neck pain and increased pain sensitivity have been established in both acute and ongoing neck pain (Javanshir et al., 2010, Sterling et al., 2002, Sterling et al., 2004). Furthermore, reorganized motor control has been demonstrated in neck pain populations (Falla, 2004). This knowledge has laid the groundwork for many different treatment strategies (Gross et al., 2015a, Gross et al., 2015b), but so far none of these have showed superior outcomes. Interestingly, a recent study indicated that simple advice was just as effective as a comprehensive rehabilitation programme, underpinning the need for a better understanding of the underlying mechanisms (Michaleff et al., 2014).

1.4. NECK PAIN – THE RELEVANCE OF THE SHOULDER GIRDLE

In recent years, the shoulder girdle has received increased attention, from both researchers and clinicians, as a possible contributing factor in ongoing neck pain. This assumed involvement of the shoulder in neck pain is based on findings of reorganized axioscapular muscle (AM) activity in populations with ongoing neck pain (Cagnie et al., 2014, Castelein et al., 2015, O'Leary et al., 2009). However, whether such changes occur immediately after the initial onset of neck pain is unknown. The theory that the shoulder girdle could play an important role in neck pain is not new. In fact, it was originally suggested in the 1980’s that due to the close anatomical link, with muscles directly linking the scapula and the cervical spine, altered AM activity during upper limb movements could induce a painful response (Behrsin and Maguire, 1986). Although this theory is plausible, and has been around for many years, the relationship between neck pain and upper limb function is still not fully understood. A recent study found that nearly 80% of those suffering from neck pain felt their pain was aggravated by upper limb activity (Osborn and Jull, 2013), which could indicate a link between shoulder movements and the sensitivity of pain mechanisms in people who suffer from neck pain. Furthermore, it is unclear whether the response to upper limb activity is different in neck pain populations compared to pain free controls. With exercises targeting AM being recommended as part of neck pain rehabilitation (Cagnie et al., 2014, Ris et al., 2016, O'Leary et al., 2009), further investigations of the relationship between the neck and the shoulder girdle are warranted.

1.5. AIMS OF THE THESIS

I) To study the sensory profile (pain and pain sensitivity) of acute and ongoing neck pain

Ia) To assess potential differences in pain sensitivity response to upper limb activity in participants with and without neck pain.

II) To investigate the potential link between neck pain and altered axioscapular muscle function.

IIa) To examine differences in adaptations of axioscapular muscle activity during an upper limb task in participants with and without neck pain.

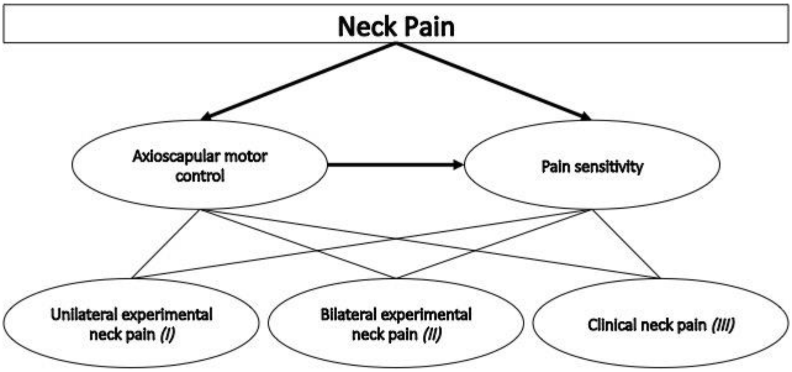

Figure 1.1 *Outline of the three studies forming the basis of this thesis with the purpose of investigating the effects of experimental and clinical neck pain on axioscapular motor control and pain sensitivity both experimentally (I, II) in healthy volunteers and in clinical populations (III).*

1.6. HYPOTHESES

The hypothesis was that acute experimental neck pain would cause increased pain sensitivity (hyperalgesia) in healthy volunteers, as well as reorganized activity of AM activity during arm movements. For populations with ongoing neck pain increased pain sensitivity (hyperalgesia) was expected when compared to healthy controls, which would be further exacerbated by upper limb activity. For muscle activity, a differentiated response with regards to AM activity was expected when comparing different neck pain groups to healthy controls.

CHAPTER 2. ASSESSING PAIN AND MUSCLE ACTIVITY

To study the effects of both acute experimental (I-II) and ongoing clinical (III) neck pain on pain sensitivity and motor control, the current studies investigated a range of different parameters, which will be presented in the following sections. Table 2.3 at the end of this chapter summarizes the methodology used.

2.1. INDUCTION OF EXPERIMENTAL NECK PAIN

Several ways of inducing experimental pain exist, ranging from injection of algetic substances to applying mechanical or electrical stimulation (Graven-Nielsen, 2006). Injection of hypertonic saline was first described in 1938 (Kellgren, 1938) and is today one of the most frequently used acute experimental pain models (Graven-Nielsen and Arendt-Nielsen, 2010). Inducing pain by injecting hypertonic saline is considered a safe way to cause a short-lasting localized and referred pain resembling what is seen in clinical pain (Schmidt-Hansen et al., 2006, Svensson et al., 1995, Kellgren, 1938). Although it remains unclear which receptors are excited following the injection of hypertonic saline, it is believed to be mediated through group III & IV nociceptive afferents (Graven-Nielsen, 2006, Graven-Nielsen and Arendt-Nielsen, 2010, Cairns et al., 2003, Mense, 2009).

There are several reasons for using experimentally induced pain by injection of hypertonic saline to investigate neck pain: firstly, it makes it possible to target a specific area in which the pain is induced; secondly, it allows for investigation of the immediate effects of neck pain after the onset, which would be nearly impossible in a clinical population; and thirdly, the effects of pain can be investigated without any potential confounding factors that might be at play in a clinical population. Previous studies investigating the effect of saline-induced pain, with the focus on AM activity during an upper limb task, have targeted the upper trapezius (Falla et al., 2007b, Falla et al., 2009, Madeleine et al., 2006, Madeleine et al., 1999). Although the upper trapezius muscle is the most commonly used site for experimental pain, it may not be an optimal model if the purpose, besides investigating pain sensitivity, is to investigate the effect of neck pain on AM activity during arm movements, since the upper trapezius muscle would be directly involved in such activity. This problem can be overcome by instead targeting the splenius capitis muscle, which is not involved in upper limb activities. This muscle has previously been targeted with saline-induced pain, though not with the purpose of investigating AM activity during arm movements (Schmidt-Hansen et al., 2006, Falla et al., 2007a, Gizzi et al., 2015, Malmstrom et al., 2013).

In the current work, the splenius capitis muscle was targeted in healthy controls using experimental painful injections (Table 2.3) of hypertonic saline (5.8%) unilaterally (I) and bilaterally (II), while isotonic saline (0.9%) was used for control injections (Falla et al., 2007a, Gizzi et al., 2015). The injection site and depth of the splenius capitis muscle was identified between the lateral border of the upper trapezius muscle and the posterior border of the sternocleidomastoid muscle at the level of the spinous process C3 (Falla et al., 2007a) using ultrasound imaging.

In summary, through an experimental acute neck pain model by injection of hypertonic saline into the splenius capitis muscle, a muscle not functionally connected to the shoulder girdle, it becomes possible to investigate the immediate effects of neck pain on sensory and motor aspects which would not be possible in a clinical population.

2.2. STANDARDISING MOVEMENTS

In the literature, there seems to be an agreement that altered function of the AM could be a contributing factor to neck pain (Cagnie et al., 2014, Castelein et al., 2015, O'Leary et al., 2009, Behrsin and Maguire, 1986). Interestingly, even though many studies have investigated pain sensitivity (Appendix A), and neck pain patients report their symptoms aggravated by upper limb activity (Osborn and Jull, 2013), no study has investigated this link between pain sensitivity and upper limb activity in a neck pain population. Studies that have considered upper limb activity in a neck pain population, have been criticised for investigating different tasks and thereby limiting the possibility for direct comparison between studies (Castelein et al., 2015). With this in mind, the current work has used the same standardised task in all studies (I-III), making it possible to compare the effects of repeated arm movements during experimental (I-II) and clinical neck pain (III). An experimental setup was adopted from a previous study (Helgadottir et al., 2011) allowing standardised slow and fast movement in the scapular plane, bilaterally (one arm at the time; Fig. 2.1; Table 2.3). Slow (I-III) and slow resisted movements (II: 1kg wrist cuff) consisted of both a 3 second up and a 3 second down phase without any pause at the top level, while for the fast movements (I-III) only the up movement was investigated.

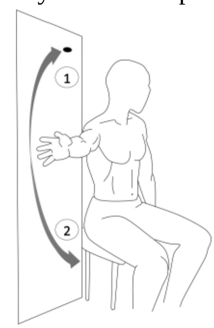

Figure 2.1 *Schematic drawing showing the experimental setup with an upwards (1) and a downwards (2) movement of the arm*

To estimate the perceived difficulty of a task, a Likert scale can be used. The Likert scale was first presented by Rensis Likert in 1932 as an easy way of quantifying the level of agreement or disagreement when answering a standardized question (Likert, 1932). In the current work (I-III) a 6-point Likert scale was used to quantify perceived difficultness of performing arm movements and went from 0 = ‘no problems’, 1 =

‘minimally difficult’, 2 = ‘somewhat difficult’, 3 = ‘fairly difficult’, 4 = ‘very difficult’, to 5 = ‘unable to perform’.

In summary, studies assessing upper limb activity in neck pain populations have been criticised for investigating different tasks. The current work has used the same task, consisting of standardised upper limb movements, in all three studies with perceived performance monitored using a 6-point Likert scale.

2.3. QUANTIFYING THE PAINFUL EXPERIENCE

In all studies (I-III) a number of different measures were used to quantify the perception of pain during the test session. Each measure is described below and summarised in table 2.3.

Pain intensity can be quantified using the visual analogue scale (VAS). The VAS scale was described for recording pain in 1974 (Huskisson, 1974) and has, since then, been used for both acute and ongoing pain, and is considered a valid and reliable way of recording pain intensity (Ferreira-Valente et al., 2011, Bijur et al., 2001, McCormack et al., 1988). In the current work (I-III), intensity of pain was recorded using a 10-cm electronic VAS scale, anchored with ‘no pain’ and ‘maximum pain’. However, the VAS scale does not assess the quality of pain. For this purpose, the McGill pain questionnaire (MPQ) was used. The original MPQ was presented in 1975 as a way to describe the quality of pain (Melzack, 1975). Since then, the MPQ has been shown to be both reliable and valid (Roche et al., 2003, Byrne et al., 1982, Hawker et al., 2011). In addition, its ability to discriminate between clinical conditions and its sensitivity to change, has made the MPQ a widely used tool in both research and clinical settings (Main, 2016). In the current work (I-III), an English (Melzack, 1975) or a Danish (Drewes et al., 1993) version of the MPQ was used to identify words describing the painful experience. Body charts are frequently used to quantify location and spatial distribution of perceived pain (Margolis et al., 1988, Fillingim et al., 2016) and were used for this purpose in all three studies (I-III). Assessing disability in neck pain was relevant in the final study (III) where clinical populations suffering from neck pain were included. For this purpose, the Neck Disability Index (NDI) was used. The NDI was first presented in 1991 as a reliable tool to assess the impact of neck pain (Vernon and Mior, 1991), and is today one of the most widely used questionnaires in research and clinical practice when assessing neck pain populations (Vernon, 2008).

In summary, a number of methods to quantify a painful experience exist. In the current work pain intensity was monitored using a 10-cm VAS scale and the quality of pain by using the MPQ, while perceived area of pain was recorded on a body chart. For the clinical populations, the NDI was used to assess the level of disability due to neck pain.

2.4. ASSESSING PAIN SENSITIVITY

Pain sensitivity has been investigated using different modalities, such as electrical (Rosen et al., 2008, Curatolo et al., 2001), thermal (Sterling et al., 2003, Wallin et al., 2012), and mechanical (Jensen et al., 1986) stimuli. Pressure pain thresholds (PPT) have been used extensively in the literature when investigating pain sensitivity in neck pain patients (Appendix A). In general, neck pain patients demonstrate increased pain sensitivity compared to healthy controls, though there are indications that this may potentially be influenced by symptom severity (Lopez-de-Uralde-Villanueva et al., 2016, Sterling et al., 2004, Sterling et al., 2003), duration (Javanshir et al., 2010), and the specific population investigated (Chien and Sterling, 2010, Scott et al., 2005). The widespread use of PPT measurements may be due to the non-invasive nature, in addition to the high levels of test re-test reliability in both asymptomatic controls and patient populations (Walton et al., 2011, Brennum et al., 1989, Prushansky et al., 2007, Vaegter et al., 2016). Deep-tissue sensitivity is thought to play an important role in many painful conditions (Arendt-Nielsen and Graven-Nielsen, 2002) and although PPT is non-invasive, it is believed to test the sensitivity of deep-tissue (Graven-Nielsen et al., 2004, Kosek et al., 1995). However, it is important to remember that the skin is deformed when conducting PPT measurements (Finocchietti et al., 2013) and some studies have found that the skin, albeit to a smaller degree, also contributes to the overall estimation of pressure sensitivity (Graven-Nielsen et al., 2004, Reid et al., 1996), while others have not (Fujisawa et al., 1999). In the current work (I-III), a handheld digital algometer (Somedic AB, Hörby, Sweden) mounted with a 1-cm^2 probe was used and the force applied was set to 30 kPa/s. This digital model has an advantage over analogue devices since the digital display helps to ensure a steadily increasing pressure force is applied, and thereby provides more accurate recordings (Rolke et al., 2005). Three standardized bilateral assessment sites were used in all studies (Table 2.1), based on the work by Kasch et al. (2001) and Slater et al. (2005).

Table 2.1 *Description of PPT sites used in study I-III*

PPT Site	Description
Neck	Over the splenius capitis muscle: midpoint between the lateral border of the upper trapezius muscle and the posterior border of the sternocleidomastoid muscle at the levels of the spinous process of C3
Head	Over the temporal muscle: Intermediate portion, above the ear.
Arm	Over the extensor carpi radialis brevis muscle, distal to the extensor aponeurosis between the extensor carpi radialis longus and the extensor digitorum muscles

In summary, pain sensitivity can be investigated using different modalities. In the current work, pain sensitivity was captured by measuring PPTs in different body locations i.e. the neck, head and arm.

2.5. ASSESSING MUSCLE ACTIVITY

Electromyography (EMG) can, in general, be divided into two different techniques commonly used when recording EMG signals, surface- and intramuscular EMG. Surface EMG is a non-invasive technique where electrodes are placed on the skin to record the activity of the muscles below. However, this method does have one major shortcoming, the risk of cross talk from other muscles, which can be minimized with optimal electrode placement, but not ruled out (Hermens et al., 2000, Disselhorst-Klug et al., 2009). One way of avoiding cross talk is with intramuscular EMG recordings, an invasive method where electrodes are inserted directly into a muscle, allowing for targeting specific muscles. Nevertheless, intramuscular EMG has been criticised for only recording from the motor units near the electrode itself and might, therefore, not be representative of the overall muscle activity (Merletti and Farina, 2009, Jaggi et al., 2009).

In the current studies, surface EMG has been used to record muscle activity during the upper limb task, which is in line with the vast majority of studies investigating this topic in neck pain populations (Appendix B). From Appendix B it is evident that the most common muscle investigated is the upper trapezius muscle, which has been studied in a variety of different tasks and populations, and has shown increased, unchanged and decreased activity. In the current work, prime movers around the scapula and shoulder girdle, along with trunk muscles, were investigated. The AM are of particular interest in the current work, since they connect the upper limb to the cervical spine (Cools et al., 2014, Pidcoe and Mayhew, 2009) and thereby enable load transfer from the upper limb to the cervical spine (Behrsin and Maguire, 1986). Trunk muscles also play an important role as they compensate for the perturbation of the trunk caused by arm movements (Hodges and Richardson, 1996), and by monitoring these during movement, it is possible to get an indication of whether postural control is affected during different conditions, such as experimental or clinical neck pain. Specific muscles investigated, along with electrode placement for the current work (I-III), can be seen in table 2.2 and were based on the SENIAM recommendations (Hermens et al., 1999), the work of Basmajian and Blumenstein (1989) along with Ng et al. (1998).

EMG recordings do not only allow for extracting root mean square (RMS) EMG as a measure of muscle activity, but also detecting the onset of muscle activity. Previously, detection of EMG onsets for local neck muscles, by either visual inspection (Falla et al., 2004b, Falla et al., 2011) or automatic detection (Boudreau and Falla, 2014), have been used in the neck pain literature. Interestingly, despite the many studies investigating AM activity in neck pain populations (Appendix B), only one previous study has investigated EMG onset for these muscles (Helgadottir et al., 2011). In the current studies (I, III) an automated approach, suggested by Santello and colleagues (Santello and McDonagh, 1998), was used in combination with visual inspection to ensure correct detection.

In summary, in the current work, surface EMG was used to estimate muscle activity (RMS EMG) and onset of eight bilateral AM, shoulder and trunk muscles during series of standardized arm movements.

Table 2.2 *Description of EMG electrode placements used in studies I-III. All electrode placements were performed bilaterally.*

Muscle	Electrode placement
Serratus anterior (SA)	In the direction of the muscle fibres at the level of 6th – 8th rib, anterior to the border of the latissimus dorsi muscle
Upper trapezius (UT)	At the midpoint on a line from the acromion to the spinous process of C7
Middle trapezius (MT)	At the level of T3 at the midpoint between the spine and the medial border of the scapula
Lower trapezius (LT)	Two thirds from the trigonum spinae of the scapula towards T8
Anterior deltoid (AD)	Approximately 2-cm anterior and distal to the acromion on a line towards the thumb (palm facing medially)
Middle deltoid (MD)	On a line from the acromion towards the lateral humeral epicondyle, over the greatest muscle bulge
External oblique (OE)	On a line between the inferior margin of the rib to the contralateral pubic tubercle, just below the rib cage
Erector spinae (ES)	Approximately 3.5-cm lateral to the L1 spinous process

Table 2.3 *An overview of the standardized methods used in the current studies*

Parameters	Methods	Standardisation
<u>Experimental pain (I-II)</u>	<u>Experimental pain</u> a. Anatomical location: Splenius capitis b. Bolus injection	<u>Experimental pain</u> a. Injection site verified using ultrasound imaging b. Hypertonic saline (5.8%) / Isotonic saline (0.9%)
Pain intensity (I-III)	Electronic VAS scale	Data recorded by PC
Painful area (I-III)	Body chart	Area manually mapped and calculated on PC
Pain quality (I-III)	McGill Pain Questionnaire	Most chosen words for each study is reported
Disability (III)	Neck Disability Index	Mean scores for all groups were reported in study III
Pain sensitivity (I-III)	Pressure Pain Threshold (PPT)	PPT recorded at three standardized sites using a digital algometer, 30kPa/s, 1-cm^2 probe
<u>Arm movements (I-III)</u> a) Standardizing movement b) Monitoring movement **c)** Perceived performance	<u>Arm movements</u> a) Scaption (30° to the frontal plane) to 140° initiated by a ‘beep’, with a ‘beep’ separating the up and down movement at 140° and a final ‘beep’	<u>Arm movements</u> a. Plexiglas wall angled 30° with marker at 140° b. Accelerometer data recorded duration of movement c. 6-point Likert scale:

	when the arm should be back at the start position. Each ‘beep’ was separated by 3-s. b) Accelerometer mounted over lateral humeral epicondyle c) Verbal Likert scale rating of perceived performance of arm movement	0. ‘no problems’ 1. ‘minimally difficult’ 2. ‘somewhat difficult’ 3. ‘fairly difficult’ 4. ‘very difficult’ 5. ‘unable to perform’
Muscle activity (I-III)	Electromyography (EMG) a) RMS EMG b) Onset	EMG recordings from 8 bilateral muscles during all movement series

CHAPTER 3. SENSORY EFFECTS OF NECK PAIN

This chapter describes some of the sensory manifestations that have been observed in both experimental neck pain in healthy volunteers as well as those seen in clinical neck pain populations.

3.1. EXPERIMENTAL NECK PAIN

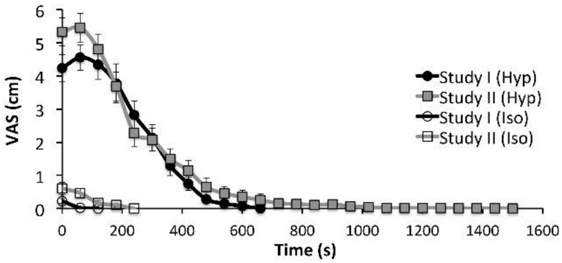

Figure 3.1 *Mean VAS score (± SEM) for hypertonic (Hyp) or isotonic (Iso) saline injected into the splenius capitis muscle in study I (N=24: unilateral injection) & study II (N=25: bilateral injection)*

The experimental pain used in the current work (I-II), by injection of hypertonic saline into the splenius capitis muscle, caused peak VAS scores and pain duration (Fig 3.1) similar to what has been seen in other studies targeting the same muscle (Schmidt-Hansen et al., 2006, Falla et al., 2007a, Gizzi et al., 2015, Malmstrom et al., 2013). Although the mean VAS score for hypertonic saline remains greater than zero for much longer during study II, compared to study I (Fig 3.1), this was due to one subject reporting a very low pain score (VAS < 0.5 cm) for a long duration. Despite this, the mean duration of pain in study II (597.6 sec ≈ 10 minutes) was still consistent with that reported by Falla and colleagues (2007a). For both studies I and II, the perceived area of pain spread further than the injection site itself (Fig. 3.2), similar to what has been found in previous studies injecting the splenius capitis muscle (Schmidt-Hansen et al., 2006, Falla et al., 2007a). Interestingly, in the current work (I; fig.3.2A) the spread of pain only reached the upper cranial area in a single subject during the experimental pain, in line with the observations by both Malmstrom et al. (2013) and Falla et al. (2007a) who reported this for only one and two participants, respectively. These findings are, however, in contrast with the

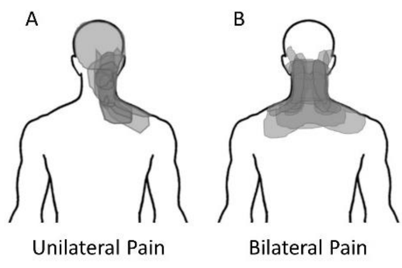

Figure 3.2: *A & B shows body chart drawings following injection of hypertonic saline in a healthy population with color transparency indicating the area was marked less frequently: A) N=24: Unilateral experimental pain, B) N=25: Bilateral experimental pain. A: Adapted from I; B: Adapted from II*

study by Schmidt-Hansen et al. (2006) where pain spreading to the upper cranial area was common. One explanation for this difference in the spread of pain between the previous study (Schmidt-Hansen et al., 2006) and the current work (I, II) may be the injection site, despite targeting the same muscle. The previous study by Schmidt-Hansen et al. (2006) injected at the midline between the external occipital protuberance and the mastoid process, making the injections site above the level of the C1 vertebra, near the insertion of the splenius capitis and other occipital muscles (Pidcoe and Mayhew, 2009) while the current work (I-II), along with that by Falla et al. (2007a) and Malmstrom et al. (2013), injected at the level of C2-C3. A more cranial, compared to a caudal, painful injection has previously been shown to cause more frequent spread outside the neck area and into to the head region (Feinstein et al., 1954, Campbell and Parsons, 1944, Bogduk and Govind, 2009). Perceived area of pain has not previously been investigated following bilateral saline-induced pain in the splenius capitis muscle, though when this has been done for the upper trapezius muscle, no side differences were observed (Ge et al., 2006).

When participants were asked to describe the quality of pain in study I, following the unilateral painful injection, the three most chosen words on the MPQ were ‘pressing’, ‘intense’ and ‘tight’ (Table 3.1). Following the bilateral injection in study II, the most chosen words were ‘taut’, ‘hot’ and ‘tight’ / ‘pressing’. Overall, the findings in the present work (I-II) are in line with those reported by Falla et al. (2007a), where ‘tiring‘ / ‘tight‘ (36%) and ‘taut‘ (29%) were the most common words, and similar descriptive words have also been reported for painful injections into other muscles (Graven-Nielsen, 2006, Graven-Nielsen et al., 1997, Ge et al., 2006).

In summary, using an experimental model of saline induced acute neck pain, the current work (I-II) caused a similar response in regards to pain intensity, perceived area, and the words used to describe the pain, as has been reported in previous studies using similar experimental models.

Table 3.1 *MPQ results from study I & II*

Study:	I	II
MPQ: Most chosen words	Pressing (38%) Intense (29%) Tight (29%)	Taut (56%) Hot (40%) Tight (32%) Pressing (32%)

3.2. CLINICAL NECK PAIN

The perceived areas of pain seen in clinical neck pain populations (III; Fig.3.3) are clearly larger than what was seen following experimental neck pain in healthy volunteers (fig.3.2). However, when examining the two figures, the majority of the neck pain patients indicated a painful area similar to that indicated by the healthy controls, with only a few who drew a larger area, as indicated by the area with the most transparent colour on figure 3.3. Spreading of the perceived area of pain is expected to happen over time following the initial onset. The exact mechanism behind such a spatial distribution is not clear but could be due to latent interneuronal connections in the dorsal horn, which may become operative when receiving ongoing nociceptive impulses, resulting in a greater area of pain than the initial one (Graven-Nielsen and Arendt-Nielsen, 2010). Interestingly, in both patient groups, an increase in the area of perceived pain was seen following repeated series of arm movements (III) which could be an effect of the ongoing and steadily increasing mean VAS score reported by the both the WAD (3.4 cm to 4.8 cm) and IONP (2.9 cm to 4.3 cm) groups during the study (III). The observed increased symptoms following upper limb movements is consistent with the findings of Osborn and Jull (2013), where neck pain patients reported their symptoms to be aggravated by upper limb activity. In regard to describing the quality of pain, the most common words from the MPQ for both neck pain groups (III) can be seen in table 3.2. Although taut was the most chosen word for both IONP (III; Table 3.2) and the bilateral saline-induced pain (II; Table 3.1), there was no other overlap when investigating the most chosen words to describe the pain experience. When comparing the chosen words from the experimental studies (I-II; table 3.1) with those from the clinical neck pain (III; table 3.2), it becomes clear that only the neck pain patients included affective aspects by choosing ‘Tiring’ and ‘Nagging’, whereas all but one word, ‘intense’, is related to sensory aspects for the experimental pain models (Melzack and Torgerson, 1971). A discrepancy between acute experimental and ongoing clinical neck pain is not surprising, and is supported by a study reporting that words describing the affective aspects of pain are more frequently chosen in ongoing pain than acute pain (Reading, 1982)

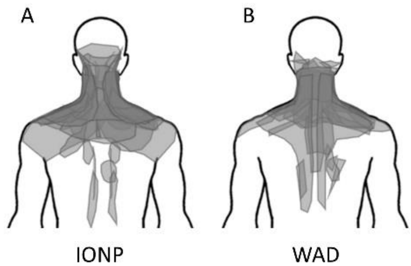

Figure 3.3: *A & B shows body chart drawings in clinical neck pain (N = 25: 16 IONP, 9 WAD) at baseline. Color transparency indicates it was marked less frequently.*

Table 3.2 *MPQ results from IONP and WAD groups in study III*

	IONP	WAD
MPQ: Most chosen words	Taut (81%) Tugging (41%) Tiring (44%)	Nagging (67%) Throbbing (56%) Tiring (56%) Radiating (56%)

In summary, the perceived areas of pain along with pain intensity was increased after repeated series of arm movements in neck pain patients (III). Although clinical neck pain had similar traits as experimental neck pain with regard to the area of pain and pain intensity, the clinical neck pain patients (III) were more prone to choose words describing affective aspects of pain compared to participants experiencing experimental neck pain (I-II).

3.3. EXPERIMENTAL PAIN & PRESSURE PAIN SENSITIVITY

The investigation of pressure pain sensitivity can help to determine the sensitivity of the nervous system when both local and distant areas (away from the painful area) are investigated (Walton et al., 2017). Localized hyperalgesia is a normal response following an injury, whereas widespread hyperalgesia is indicative of facilitated central processing caused by ongoing nociceptive stimuli (Graven-Nielsen and Arendt-Nielsen, 2010, Woolf, 2011). The need for ongoing nociceptive input to cause widespread changes is in line with findings of a study showing that only ongoing, and not acute neck pain, elicited widespread changes (Javanshir et al., 2010). When investigating PPT in a healthy population during short-lasting experimental pain, such widespread hyperalgesia is not expected. In fact, previous studies investigating PPT responses following a single injection of hypertonic saline into the neck area of healthy participants have failed to see any significant widespread responses (Schmidt-Hansen et al., 2006, Ge et al., 2003), while a hypoalgesic response has been observed following bilateral injections, but only in the surrounding area of the injection site (Ge et al., 2006, Ge et al., 2003). This is, to some degree, in line with the current findings where unilateral injections caused no significant changes in pain sensitivity when compared with the control condition (I), but the bilateral injections (II) lead to a significant hypoalgesic effect at the head and arm site (fig. 3.4). Ge and colleagues (2003) interpreted the decreased pressure pain sensitivity observed distant to the injection site as a sign of normal descending pain modulation, where only the spatial summation of two noxious stimuli were enough to trigger this response, while the unchanged local PPTs were explained as a balance between local hyperalgesia following the injection and the elicited hypoalgesia. In contrast, following the bilateral injections in the current work (II), a local hyperalgesic effect was observed for the post condition (5-min after pain had vanished), which is similar to what has been observed in other studies investigating experimental pain in other body regions, such as the shoulder (Domenech-Garcia et al., 2016) or the pelvic girdle (Palsson and Graven-Nielsen, 2012, Palsson et al., 2015). While the literature seems to be in agreement with the responses seen distant to the injection site, the mixed findings in the local area are not easily explained. One possible explanation might simply be the different locations of injection and thereby different tissue properties, such as the density of vascularization and innervation. Palsson et al. (2012) argued that hyperalgesia following hypertonic saline injections into ligaments could be the effect of a poor ability to remove “sensitizing agents” from the tissue. With this in mind, it might be possible that a larger muscle, like the trapezius, might allow for better absorption or removal of sensitizing agents following injection, compared to a smaller muscle like the splenius capitis.

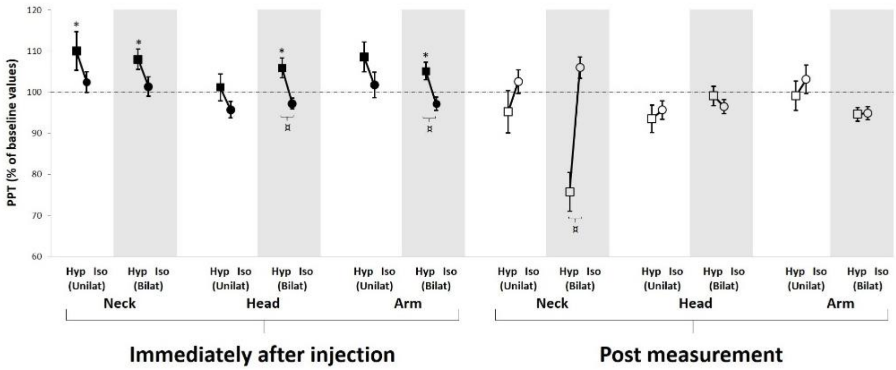

Figure 3.4 *Mean normalized PPT (± SEM) recorded over the splenius capitis (Neck), temporalis (Head) & extensor capitis radialis brevis (Arm) muscles immediately following either unilateral (Unilat: PPT recorded on the injection side; N=24) or bilateral injections (Bilat: mean of bilateral recordings; N = 25) of hypertonic (□ Hyp) or isotonic (○ Iso) saline. Filled markers = Immediately after injection. Open marker = Post session 5-min after any potential pain had vanished. ¤ Significant difference compared with isotonic saline or * to post measurement of same condition (NK: P < 0.05).*

In summary, the current work indicates that only bilateral (II), and not unilateral (I), saline-induced pain caused a remote hypoalgesic effect, in line with a previous study using a similar experimental pain model (Ge et al., 2003). Furthermore, only the bilateral model (II) produced a significant local hyperalgesic effect during the post-pain measurement which contrasts previous studies using similar pain models within the neck area.

3.4. CLINICAL PAIN & PRESSURE PAIN SENSITIVITY

A common finding when comparing neck pain populations to healthy controls, is locally reduced PPT measurements in the neck area, with some also showing widespread hyperalgesia (Appendix A). Local reduction in PPT is considered to be a normal reaction following injury to a muscle or joint, whereas widespread decreased PPTs observed in some neck pain populations are considered to be a sign of facilitated central processing of noxious stimuli (Sterling, 2008, Scott et al., 2005, Sterling et al., 2002). Facilitation of central pain mechanisms develops over time following a sufficiently intense and ongoing noxious stimulus and the mechanism behind this phenomenon has been proposed to be an imbalance between facilitated responses to nociceptive input, with increased response compared to what is normal, and reduced descending inhibitory effects on pain (Graven-Nielsen and Arendt-Nielsen, 2010, Yarnitsky, 2010, Woolf, 2011). This is in line with clinical findings demonstrating that ongoing non-acute neck pain patients display widespread hyperalgesia (Javanshir et al., 2010, Sterling et al., 2002). However, in addition to the duration of the noxious stimulus, the intensity also seems to play a key role for central changes to takes place, based on a study on acute WAD showing that widespread changes were only present in those suffering from moderate to severe but not mild symptoms (Sterling et al., 2004). Although it has been suggested that widespread hyperalgesia may only be a feature of WAD but not IONP (Scott et al., 2005, Coppieters et al., 2017), the current work (III) along with that of Javanshir et al. (2010) indicates that this may not be the case, as widespread reductions in PPTs are found in both IONP and WAD groups (Fig.3.5). However, when comparing the reported pain intensities in the study by Scott et al. (2005), the WAD group had a mean VAS score of 3.2-cm, which is closer to the observations for both neck pain populations in the current work (III), than the VAS 2.4-cm they found for their IONP group. Similar differences were observed between groups, using an 11-point numeric rating scale (NRS), in the study by Coppieters et al. (2017) with IONP reporting a mean NRS of 3.88 while the WAD group reported a mean NRS of 5.66. The reported lower pain intensity for IONP patients compared to WAD in the study by Scott and colleagues (2005), along with that of Coppieters et al. (2017), might not have been of a sufficient intensity to cause widespread changes as seen in the current work (III).

In summary, clinical neck pain can cause both local and widespread reductions in PPT. When comparing the results from different studies there is an indication that pain intensity might need to reach sufficient intensity to cause widespread changes.

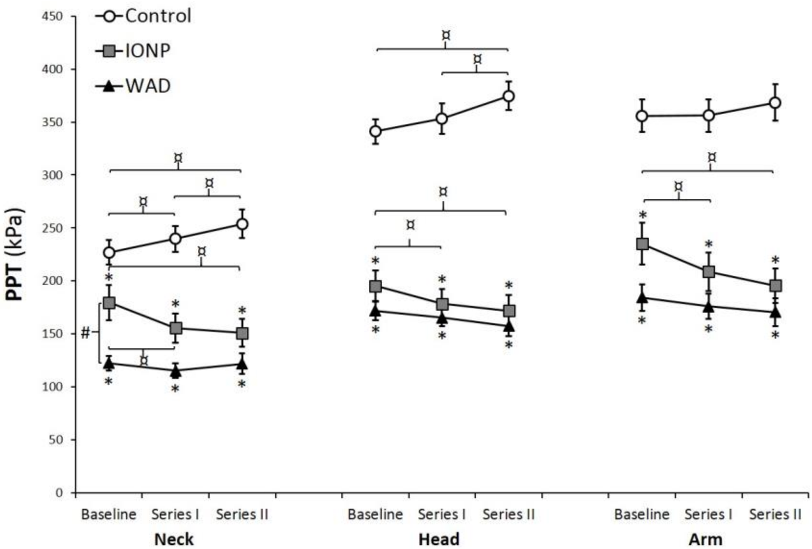

Figure 3.5 *Mean normalized PPT (± SEM) recorded over the splenius capitis (Neck), temporalis (Head) & extensor capitis radialis brevis (Arm) muscles at baseline, after exercise series I and II. * Significantly different compared to controls, ¤ within group or # between IONP and WAD (NK: P < 0.05).*

3.5. EXERCISE INDUCED EFFECTS ON PAIN SENSITIVITY

Although the theory of upper limb function being linked to neck pain has been around since the 80´s (Behrsin and Maguire, 1986) and is supported by patient reports (Osborn and Jull, 2013), many studies investigating this link have mainly focused on muscle activity (Appendix B) and not pain sensitivity. The current work (III) is the first looking specifically at the effect of standardized repeated arm movements on pain sensitivity in neck pain patients. It was demonstrated that these movements not only caused increased pain intensity and expansion of the painful area, but also had an impact on widespread pain sensitivity. For the IONP group, a significant and progressing hyperalgesic effect was observed following repeated arm movements when comparing exercise series' I and II to baseline (Fig.3.5; III). This was observed for both the neck and distant sites, while a similar but non-significant tendency was seen at the distant sites for the WAD group (III). Previous studies have shown a hyperalgesic effect of exercise with reduced PPT values in both neck pain (Van Oosterwijck et al., 2012) and fibromyalgia patients (Kosek et al., 1996, Staud et al., 2005), while healthy controls in both studies exhibited a hypoalgesic effect of exercise (EIH), which is similar to what was seen in the current study (III). The lack of EIH in patients with ongoing pain has been suggested to be due to peripheral sensitization (Kosek et al., 1996) and/or abnormal pain modulation (Kosek et al., 1996, Staud et al., 2005) with the latter being a common finding in ongoing painful conditions (Yarnitsky, 2010). Pain modulation has often been investigated by testing pain sensitivity at baseline, then adding a conditioning painful stimulus, after which a decrease in pain sensitivity is observed in healthy controls. This effect is termed conditioned pain modulation (CPM) (Yarnitsky et al., 2010). A decreased CPM effect and increased pain sensitivity have been linked to reduced EIH in pain patients (Vaegter et al., 2016, Fingleton et al., 2016). Similar observations have been made in healthy controls, with those displaying a poorer CPM effect also having less pronounced EIH (Lemley et al., 2015). Although EIH has been linked to CPM, and is believed to share similar components via the endogenous pain modulatory system, the two phenomena may not be the same. Whilst a CPM response is thought to rely on a painful "trigger", EIH can be induced without pain but the effect is less pronounced (Ellingson et al., 2014). It is known that non-painful exercise can cause EIH in neck pain, as seen by an immediate increase in PPTs locally at the neck area, following non-painful neck exercises (O'Leary et al., 2007) or exercise of non-painful muscles (Smith et al., 2017). Smith and colleagues (2017) found an EIH response in both healthy controls and a WAD group following an isometric exercise, but not after a submaximal cycling task. Similarities between the WAD group and healthy controls, observed in the study by Smith et al. (2017), has been suggested to be due to low pain levels in the WAD group and similar CPM responses for both groups (Vaegter, 2017). In contrast, a study by Van Oosterwijck et al. (2012) found a widespread hyperalgesic response, in addition to increased pain levels, in a WAD group following a bike exercise at submaximal intensity (75% of the age-predicted maximal heart rate). However, when the exercise was self-paced, a hypoalgesic effect was observed locally at the calf, indicating that the exercise intensity might be of importance (Van Oosterwijck et al., 2012). The conflicting findings reported by Van Oosterwijck et al. (2012) compared with Smith et al. (2017) could be explained by differences in the clinical populations investigated. Even though both studies investigated WAD groups, Smith and colleagues (2017) reported a more localized area of pain, along with a lower mean VAS score of 2.9-cm, while Van Oosterwijck et al. (2012) reported mean VAS scores above 5-cm, along with a fair proportion of subjects (31.8%) reporting widespread pain. A reduced CPM effect in some pain patients, indicating a less efficient pain modulatory system, could explain why some do not tolerate high intensity exercise and hence demonstrate a hyper- instead of a hypoalgesic effect. This is in line with a recent study showing that even within a population suffering from ongoing pain, large variation exists in the efficiency of the pain modulatory system, which should be considered when choosing an intervention (Vaegter et al., 2016). In the current work (III), the exercise intensity might have been near submaximal for some of the neck pain patients as 25% from the IONP group and 67% from the WAD felt increased difficulty lifting the arm, which could explain why hyper- and not hypoalgesia was observed. Unlike the IONP group, no additional decrease in PPT at the neck site was observed for the WAD group, which could be explained by a floor effect, as the WAD group displayed very low baseline values (III). Another possible explanation for the non-significant changes over time displayed by the WAD group (III) could be the limited sample size.

Although the current work (III) showed increased symptoms following repeated arm movements, there are studies on patient populations showing benefits both immediately after exercise and from a long term exercise program. Although the initial hypoalgesic effect following exercise reported in some studies is short lived (Vaegter et al., 2014), hypoalgesic effects have been observed following exercise programs continued over several months in populations with neck and shoulder pain (Andersen et al., 2012, Karlsson et al., 2015). This, in combination with the findings suggesting that intensity of exercise may influence the subsequent EIH response (Van Oosterwijck et al., 2012), indicates that neck pain patients will benefit from exercise, but the intensity may need to be tailored to the individual patient. Such an individually tailored approach is in line with recommendations by Vaegter et al. (2016), stating that clinicians should evaluate the pain modulatory system for each patient when considering treatment options.

In summary, ongoing painful conditions have, in different studies, shown to impact on the efficacy of pain modulation. Where healthy controls are reported to display hypoalgesia following exercise, patients display reduced or hyperalgesic responses. The results of the current work (III) indicate that the response to exercise varies between neck pain patients, though a floor effect and the limited sample size have to be considered when interpreting these results.

CHAPTER 4. MOTOR EFFECTS OF NECK PAIN

Neck pain and altered motor control have been linked in the literature. Studies of muscles in the cervical region have found reorganized muscle activity for deep and superficial neck flexors and extensors, in both experimental (Cagnie et al., 2011a, Cagnie et al., 2011b, Falla et al., 2007a) and clinical neck pain (Falla et al., 2011, O'Leary et al., 2011, Jull et al., 2004). In addition to the altered function of local neck muscles, reorganization of AM activity has also been proposed to play an important role in ongoing neck pain, as muscles like the upper trapezius and levator scapulae directly link the scapula to the cervical spine (Cagnie et al., 2014, Castelein et al., 2015, O'Leary et al., 2009). Muscle adaptations in the presence of pain are a normal response, but if this outlasts the cause of the initial pain, it becomes maladaptive and could potentially contribute to ongoing pain rather than to relieving it (Hodges and Tucker, 2011). This chapter will present the current findings for the link between neck pain and altered AM activity.

4.1. EXPERIMENTAL NECK PAIN AND MOTOR EFFECTS

While previous studies have investigated alterations in AM activity during upper limb tasks in patients suffering from ongoing neck pain (Appendix B), only a few studies exists which have investigated the effect of acute experimental neck pain on such tasks in healthy volunteers (Falla et al., 2007b, Falla et al., 2009, Madeleine et al., 2006, Madeleine et al., 1999). Despite investigating different activities, such as isometric (Falla et al., 2009, Madeleine et al., 2006) or repetitive upper limb tasks (Falla et al., 2007b, Madeleine et al., 1999), all studies found reduced activity of the upper trapezius muscle where experimental pain was induced. Such an adaptation, with reduced activity in the presence of pain, is natural and in line with the overall goal of protecting against further pain or injury (Hodges and Tucker, 2011, Hodges, 2011). However, since pain was directly induced in the muscle investigated, it may not be the best indicator of what AM adaptations could take place immediately after the onset of clinical neck pain. This is where the present work (I-II) adds new knowledge to the area, since pain was induced into a different neck muscle than what was investigated and not functionally involved in or contributing to shoulder movements. Interestingly, one of the most consistent findings in study I & II was reduced activity of the ipsilateral upper trapezius during arm movements (Fig. 4.1) following saline-induced pain into the splenius capitis muscle. Although the role of the referred pain in the area with regards to this decreased activity cannot be determined, these studies indicate that neck pain alone can cause altered AM activity. When two painful injections were given (II), instead of just one (I), a more pronounced reduction in activity was

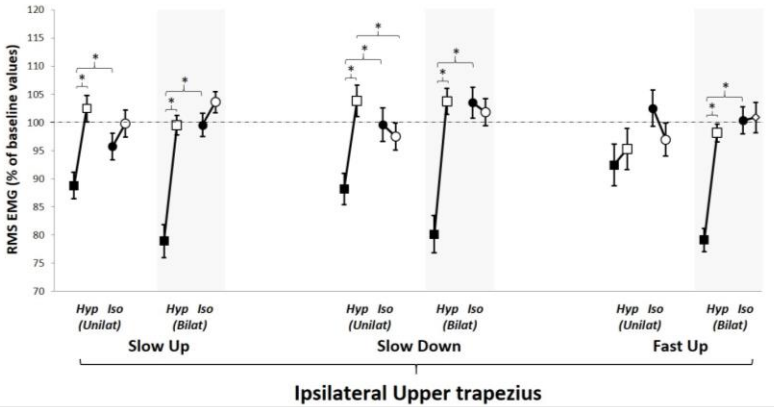

Figure 4.1 *Mean normalized RMS-EMG (± SEM) during arm movements for the ipsilateral upper trapezius muscle immediately following either unilateral (Unilat; N=24) or bilateral injections (Bilat; N = 25 for slow & N = 23 for fast movements) of hypertonic (□ Hyp) or isotonic (○ Iso) saline. Filled markers = Immediately after injection. Open marker = Post session 5-min after any potential pain had vanished. RMS-EMG recordings is depicted for slow up, down and fast up arm movements. * Significant difference (NK: $p < 0.05$).*

observed for the ipsilateral upper trapezius muscle. This is in line with a previous study on experimental knee pain showing that only bilateral, and not unilateral, experimental pain was able to cause significant changes in muscle activity (Hirata et al., 2012). Interestingly, the study by Madeleine and colleagues (1999) did not find other changes during the experimental pain besides the reduced activity for the upper trapezius muscle; whereas Falla and colleagues (2007b) found simultaneous increased activity of the ipsilateral lower trapezius muscle. In the current studies (I-II), no such changes were observed for the lower trapezius muscle, but instead increased activity was seen for the ipsilateral deltoid muscle during some movements. There may be several explanations for these different findings in different studies, with the most obvious being that not all studies monitor the same muscles and that different tasks are investigated, making it difficult to compare findings between studies. Additionally, there is no universal solution for a task, such as moving the arm during acute pain. For this reason everybody may have a slightly different approach in regards to redistributing muscle activity, within and between muscles. An individualized response to acute pain is supported by experimental pain studies conducted in both the neck (Gizzi et al., 2015) and low back regions (Hodges et al., 2013), showing that when considering multiple muscles during a movement task following saline-induced pain, no participant displays exactly the same patterns of reorganised activity compared to baseline. An individual response is also supported by the new pain adaptation theory, suggested by Hodges and Tucker (2011), stating that in an effort to protect against further pain, muscle activity can, on an individual basis, be redistributed between or within muscles. With regards to the latter potential within-muscle changes, the current work cannot account for this as only one pair of electrodes was used to monitor each muscle. However, previous studies have observed such changes within the upper trapezius muscle during a painful condition compared to no pain (Madeleine et al., 2006, Falla et al., 2009), thereby indicating that complex adaptations may take place within a muscle during a painful condition. Such changes may also be likely for the serratus anterior muscle which has anatomically separate subdivisions (Webb et al., 2016). It has been indicated that subdivisions of the serratus anterior muscle may be more or less active depending on the movements performed (Ekstrom et al., 2004), and with this in mind, it seems plausible that such a pattern might be disturbed during pain. Such speculations are, however, outside the scope of the current work.

For the first time, the current work (I-II) demonstrates a link between acute experimental neck pain and altered trunk muscle activity. Interestingly, during the bilateral neck pain (II), increased activity was observed for the bilateral erector spinae muscles (Fig.4.2). If such changes had only been seen on the contralateral side to pain, it could have indicated an effort to unload the painful side. Although this cannot be ruled out, the bilateral increase suggests this is not the case. Hodges et al. (2011) have suggested that muscle adaptations altering spinal stiffness could be a strategy to protect the spine, which is supported by observations in both experimental (Hodges et al., 2013) and clinical low back pain (van der Hulst et al., 2010). Such mechanisms, with increased muscle activity as a protective strategy, has also previously been suggested for both axioscapular- and trunk muscles in neck pain populations (Falla et al., 2017, Juul-Kristensen et al., 2013). Another explanation, suggested by Palsson and colleagues (2015), is that pain might simply lead to an overestimation of the force needed to perform a motor task, thereby accounting for the increased activity seen in a painful condition. In reality, it might very well be a combination of the two, that the force needed cannot be precisely estimated due to the pain and therefore the system increases muscle activity as a 'safeguard' to protect the spine from further harm. Whether it is one or the other or a combination of both remains unknown. The current

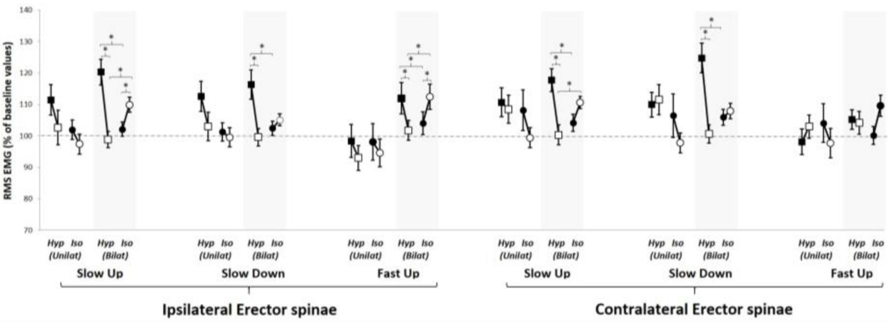

Figure 4.2 *Mean normalized RMS-EMG (± SEM) for the erector spinae muscle (ipsilateral & contralateral to movement) immediately following either unilateral (Unilat; N=24) or bilateral injections (Bilat; N = 25 for slow & N = 23 for fast movements) of hypertonic (□ Hyp) or isotonic (○ Iso) saline. Filled markers = Immediately after injection. Open marker = Post session 5-min after any potential pain had vanished. RMS-EMG recordings is depicted slow up, down and fast up arm movements. * Significant difference (NK: $p < 0.05$).*

findings warrant further investigation of muscle adaptations to pain, while simultaneously making 3 dimensional (3D) recordings of trunk movements, to illuminate the nature of such changes.

Although the present work has shown alterations in AM and trunk muscle activity as a result of experimental neck pain, no significant reorganization was observed for the onset of muscle activity during unilateral (I) or bilateral experimental neck pain (unpublished data; Fig.4.3). No other experimental neck pain studies have investigated onset of AM or trunk muscles during arm movements. However, onsets have been investigated in experimental low back pain, where Hodges et al. (2003) demonstrated delayed onset of trunk muscles during rapid arm movements following saline-induced muscle pain. These differing findings in trunk muscle onset, from the previous LBP study (Hodges et al., 2003) compared to the current work, might be explained by the previous study investigating muscles near to where pain was induced, where the current work (I-II) investigated muscles distant to where pain was induced.

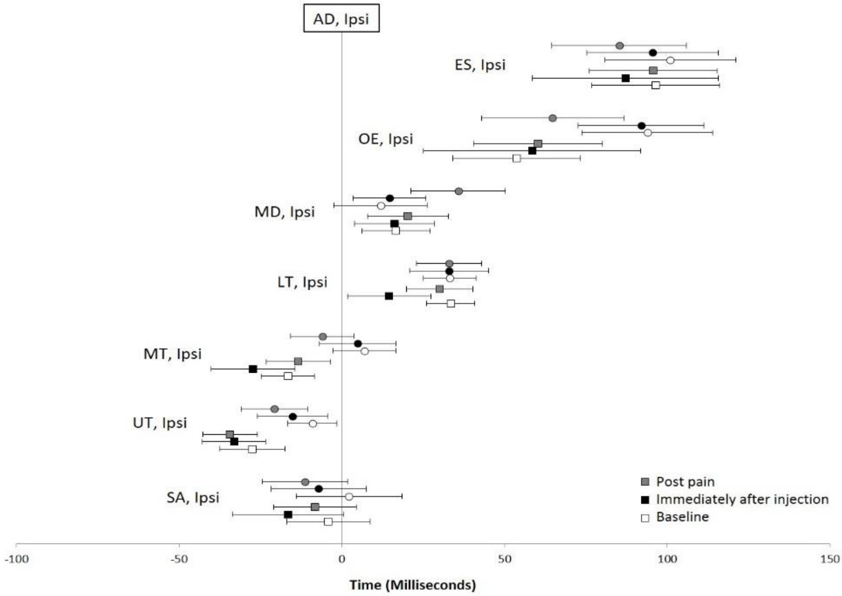

Figure 4.3 *Unpublished data: Mean (± SEM, N = 23) onset values for ipsilateral muscles during fast up movements at baseline, immediately after injection of hypertonic (□) or isotonic (○) saline and 5-min after any potential pain had vanished. Onsets are normalized to the ipsilateral anterior deltoid. Onsets were recorded from serratus anterior (SA), upper trapezius (UT), middle trapezius (MT), lower trapezius (LT), anterior deltoid (AD), middle deltoid (MD), external oblique (OE), and erector spinae (ES) muscles.*

In summary, the present experimental studies (I-II) are the first to show that pain from a neck muscle not functionally connected to the shoulder may result in a reorganisation of AM activity during upper limb movements. Such changes were seen for the upper trapezius muscle, where significant reductions in muscle activity were observed. Another novel finding of the current work is the effect of acute neck pain on *trunk muscle activity, such as the increased activity observed for the erector spinae muscles (II) which have not previously been investigated. The current work also indicates that altered AM function may occur early in clinical neck pain, based on the findings that in acute experimental neck pain changes occur within minutes of the painful onset.*

4.2. CLINICAL NECK PAIN AND MOTOR EFFECTS

Several studies have investigated AM activity in neck pain populations and shown a link between neck pain and reorganized muscle activity, though there are contrasting findings with regards to the direction of these changes depending on the muscle, task and population investigated (Appendix B). One explanation for different findings between studies could be the large diversity in the included populations. For instance, many studies have focused on trapezius myalgia or included participants with shoulder or arm pain, rather than focusing only on pain from the neck, making it hard to determine a potential cause and effect relationship. Pain in the shoulder or arm can arise from the neck (Dalton and Jull, 1989), but there are also reports of shoulder problems causing pain in the neck area (Gorski and Schwartz, 2003). Furthermore, shoulder pain on its own is thought to be able to reorganize AM activity (Kibler and McMullen, 2003). Due to this unclear relationship between neck pain and altered AM function (Cools et al., 2014), it is difficult to determine what came first. If the purpose is to assess the effect of neck pain on AM activity it may be necessary to look aside from studies including participants with symptoms from the shoulder, arm or trapezius myalgia. In the current work (III), only participants with pain arising from the neck were included, though referred pain outside the neck area was also observed. Although participants had to have pain free shoulder movement and neck pain patients with shoulder or arm pain were excluded from the study (III), this does not rule out the presence of reorganized AM activity before the onset of neck pain. It did, however, limit the possibility of shoulder or arm pain contributing to the potential reorganization of AM activity. Furthermore, when comparing findings from different studies, it is important to note that even though seemingly similar populations are investigated, such as IONP, the in- and exclusion criteria may not always be the same (Castelein et al., 2015, Damgaard et al., 2013).

One of the muscles that has been the investigated extensively is the upper trapezius muscle (Appendix B), where contrasting findings of reduced (Andersen et al., 2008, Schulte et al., 2006), increased (Leonard et al., 2010, Johnston et al., 2008c) or unchanged (Nederhand et al., 2002, Elcadi et al., 2013) activity have been reported during upper limb tasks in neck pain patients when compared to healthy controls. However, when excluding studies which included participants reporting pain from the shoulder or arm, which may have contributed to the findings, there is only one study which reports changes in the upper trapezius muscle, namely an increased duration of muscle activity during upper limb activity (Tsang et al., 2014). Even studies of patients with neck pain alone, displaying altered scapular control, have not found changes for the upper trapezius muscle (Castelein et al., 2016, Wegner et al., 2010, Zakharova-Luneva et al., 2012). This is in line with the current study (III), which did not find any changes in the upper trapezius muscle. However, the previous studies including participants already displaying altered scapular control did find changes for both the middle trapezius muscle, with reduced activity (Castelein et al., 2016), and the lower trapezius muscle, with either increased (Zakharova-Luneva et al., 2012) or decreased activity (Wegner et al., 2010), during upper limb activity when compared to healthy controls. These previous findings for the middle- and lower trapezius muscles contrast the non-significant findings for these muscles in the current work (III). The only significant finding in muscle activity in the current work (III) was for the serratus anterior muscle (Fig.4.4), where increased activity was recorded for the WAD group during a movement series with short resting time, which was interpreted as a sign of fatigue. The involvement of the serratus anterior muscle in neck pain is supported by previous findings from Helgadottir and colleagues (2011), who showed that duration of muscle activity was reduced for neck pain patients, compared to controls, during a similar movement task to that used in the current work (III).

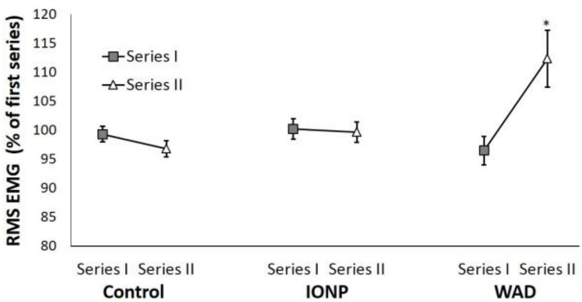

Figure 4.4 *Mean (± SEM, N = 50; 16 IONP, 9 WAD, 25 Control) normalized RMS-EMG for the ipsilateral serratus anterior muscle during a 3-sec. slow up movement over two exercise series (3 series of arm movements where the last 2 series is normalized to the 1st): Series I (movement series separated by approx. 8-min) and Series II (movement series separated by approx. 42-s). * Significant difference within and between groups (NK: P < 0.05).*

The literature within this area (Appendix B) seems to show a clear indication of neck pain being linked to altered AM activity despite that there are contrasting findings. When trying to understand these different findings, it is important to consider that different methodologies were used in the individual studies e.g. the task investigated and the method used to analyse data (Castelein et al., 2015). With regard to investigating muscle activity, many studies have normalized RMS EMG to a standardized task or a maximal voluntary contraction (MVC) specific for that single study, making it difficult to compare findings between studies (Castelein et al., 2015). Furthermore, normalising to a standardized task or MVC has been criticised when used in patient populations, as the participating individuals may already be affected by altered motor control, which could have an impact on the findings (van Dieen et al., 2003, Castelein et al., 2015). Others have chosen to look at the duration of muscle activity (Tsang et al., 2014, Helgadottir et al., 2011), while the current work has normalized to a baseline recording for investigating muscle activity (I-III). This method allows for investigating changes over time during repeated movement series, but comes at the cost of being unable to account for potential differences at baseline. Furthermore, when comparing the results of studies on acute (I-II) and ongoing neck pain (Appendix B, III), some considerations need to be given to the nature of pain and that acute pain may not be directly comparable to ongoing pain when it comes to motor control adaptations. Madeleine, P. (2010) argues that as pain changes over time, so too will the muscular adaptations. To date, there are no studies illuminating such changes during the transition from acute to ongoing neck pain, and future experimental and clinical studies are needed to clarify what changes in muscle adaptation take place.

With regard to onset of AM activity during arm movements in clinical neck pain, only the current work (III) and that of Helgadottir et al. (2011) have investigated this. The study of Helgadottir el al. (2011) found a delayed onset of the serratus anterior muscle during arm movements, which is in contrast to the current work on clinical (III) and experimental (I-II) neck pain. With no other studies having investigated the onset of AM during arm movements, there is no simple explanation for these different findings between the previous study by Helgadottir and colleagues (2011) and the current work (III) conducted on seemingly similar neck pain populations.

In summary, from the clinical study (III) an increased activity was observed for the serratus anterior muscle when repeated exercise series were conducted. The involvement of the serratus anterior muscle in clinical neck pain is supported by a previous study (Helgadottir et al., 2011) using a similar setup as the present study (III). In general, the different findings with regards to AM activity in different studies have been attributed to the different methodology used, including tasks investigated as well as differences in in-/exclusion criteria (Castelein et al., 2015). Considering these methodological differences, in addition to the small sample sizes used both in the current (III) and most previous studies (Appendix B), and the presence of potential individual differences (Gizzi et al., 2015), it is not surprising that inconsistent findings exist within the literature.

CHAPTER 5. CLINICAL IMPLICATIONS AND PERSPECTIVES

5.1. CONCLUSION AND CLINICAL IMPLICATIONS

In this thesis, a model of acute experimental neck pain has been investigated (I-II) and similar features to those observed in clinical neck pain were found (III). The current work thereby provides a way of investigating what changes may take place during the very first minutes following an acute onset of neck pain. There are, however, limitations to such a model and it is still unclear how findings in pain sensitivity and motor control adaptations from acute neck pain translate into the ongoing symptoms seen in clinical populations. From the neck pain literature it is evident that not all neck pain patients react similarly, even though they are exposed to the same stimuli, which is in line with the findings of the current work (III). Widespread hyperalgesia was seen in both neck pain populations when compared to healthy controls. Interestingly, a hyperalgesic response was seen as a response to repeated arm movements in IONP but not WAD patients, while a hypoalgesic response was seen for healthy controls (III). Such findings indicate that not all react similarly to low level exercise, even though the stimuli is the same. Evidence indicating that altered pain modulation might be the underlying reason for these findings has been presented.

For the first time, a direct link between neck pain and reorganized AM activity has been demonstrated, where the upper trapezius muscle consistently demonstrated reduced activity during arm movements in both unilateral and bilateral (I-II) experimental neck pain. These immediate changes in response to pain, underpin that motor changes seen in ongoing neck pain conditions may start already in the acute phase following onset of pain. Moreover, in a clinical neck pain population (III) an increased activity of the serratus anterior muscle was found following repeated series of arm movements, which was interpreted as a sign of fatigue. Previously, no other studies have investigated trunk muscle activity during arm movements in participants with neck pain, and hence the current work has demonstrated, for the first time, that there is a link between acute neck pain and increased trunk muscle activity such as what was seen for the erector spinae muscles (II).

Taken together, the current work (fig. 5.1) clearly supports the need to include the shoulder girdle during assessment and rehabilitation of neck pain patients. Additionally, the present findings indicate that similar considerations should be given to the trunk muscles, since they may also be affected by the painful condition. Finally, these studies, alongside previous investigations, indicate that pain sensitivity plays an important role in neck pain patients.

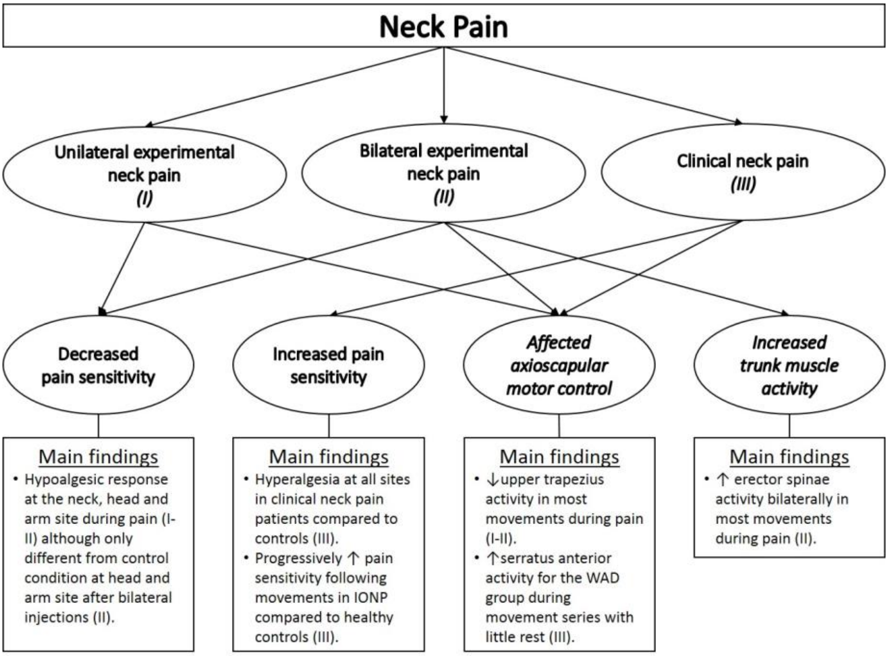

Figure 5.1 *Outline of the main findings from the three studies forming the basis of this thesis. It is seen that, although both experimental (I, II) and clinical neck pain (III) can cause altered axioscapular motor control, there are contrasting findings in regards to pain sensitivity. Here, the experimental neck pain caused decreased sensitivity while clinical neck pain caused increased pain sensitivity.*

In conclusion, clinicians need to consider both motor and sensory changes in neck pain patients when planning a rehabilitation strategy, with the emphasis on tailoring the right treatment to the right patient.

5.2. FUTURE PERSPECTIVES

The current work demonstrated that repeated arm movements further increased pain sensitivity in neck pain patients (III). Although the current work could only elicit a hyperalgesic response, other studies have seen a hypoalgesic effect following exercise. Future studies with larger sample sizes are needed to investigate a potential dose response relationship, both within a single session and over time, with the overall goal of informing clinical decision making in the rehabilitation of neck pain patients.

Future studies investigating the effect of neck pain on the motor control of AM and trunk muscles would benefit from combining 3D movement analysis with EMG recordings to investigate potential kinematic changes alongside reorganized muscle activity. Furthermore, additional studies investigating how deeper muscles, such as the levator scapula and the pectoralis minor, which are also involved in arm movements with and without pain, are warranted to get the complete overview of the effects of neck pain on motor control. In general, the majority of studies investigating motor control changes in clinical neck pain populations (including the current work) have a limited clinical sample size and futures studies should aim to rectify this. Lastly, although the current work has focused on physical parameters of neck pain, it must not be neglected that neck pain is a complex problem consisting of both bio-psycho- and social aspects. Future studies should strive to implement all of these biopsychosocial elements, with the aim of understanding why some patients recover while others do not following the initial onset of neck pain.

APPENDICES

Appendix A. A summary of studies investigating PPT in clinical neck pain

Appendix A. A summary of studies examining pressure pain thresholds in neck pain patients compared with healthy controls. * Including neck AND shoulder pain; ¤ Including arm pain; § Studies including neck pain of less than 3-months duration AND/OR without daily symptoms; # Participants diagnosed with trapezius myalgia; ʌ Patient group not clearly defined. Studies with undefined PPT sites or no control groups have been excluded. Whiplash associated disorders (WAD), Insidious onset of neck pain (IONP), Neck pain (NP= mix of different types), Neck and shoulder pain (NSP), Trapezius myalgia (TM), Healthy controls (CON).

Reference	Study Population	Aim of Study	Intervention/ Task Investigated	PPT Sites	Main Findings
(Chien and Sterling, 2010)	WAD grade II (n=50): Mean age 37.2 years (SD 10.4) IONP (n=28): Mean age 32.3 years (SD 8.7) CON (n=31): Mean age 31.4 years (SD 8.9)	To compare thresholds to sensory stimuli for IONP, WAD and CON.	No intervention.	Articular pillars of C5/C6 (Cx) Median nerve trunk near the elbow (MN) Tibialis anterior (TA) (Bilateral: 1-cm^2 probe 40 kPa/s)	No side difference was found. For both Cx & MN the neck pain groups displayed significantly lower PPTs compared to CON. For TA the WAD group had lower PPTs than both IONP and CON.
(Coppieters et al., 2017)	WAD grade II (n=32): Mean age	To investigate sensitization and disability in	No intervention.	Upper trapezius (UT)	WAD had lower PPT at all sites compared to CON, while this

	36.00 years (SD 10.79) IONP (n=35): Mean age 35.66 years (SD 10.80) CON (n=28): Mean age 31.96 years (SD 13.36)	WAD and IONP compared to CON.		Quadriceps (QC) Web between thumb and index finger (TI) Lateral to L3 (L3) (Most painful or dominant side: Increments of 1kgf)	was only the case for UT in the IONP group. No differences between IONP and WAD were observed.
¤Λ(Falla and Farina, 2005)	IONP (n=19): Mean age 38.1 years (SD 9.5), CON (n=9): Mean age 34.8 years (SD 4.9)	To compare time dependent changes in muscle fiber conduction velocity for the upper trapezius muscle during a repeated movement task in IONP and CON.	From a sitting position participants were asked to tap their hands between their mid-thigh and a target in front of them reached with a fully extended arm in 120° shoulder flexion at 88 beats/min for up to 5 min. PPTs were recorded prior to the upper limb task.	Upper trapezius (UT) (Bilateral: 1-cm^2 probe 40 kPa/s)	Bilateral PPTs were significantly reduced in the IONP group compared to CON.

*§∧(Hagg and Astrom, 1997)	NSP (n=9): Mean age 37.8 years (SD 8.2) CON (n=14): Mean age 36.9 years (SD 8.7)	To investigate possible differences in PPT and EMG gaps between office workers with and without NSP.	No intervention.	Upper trapezius (UT) Sternum (ST) (Bilateral for UT: 1-cm^2 probe 25 kPa/s)	The NSP group displayed significantly decreased bilateral PPTs for UT but not ST when compared to CON.
*§∧(Javanshir et al., 2010)	Acute IONP (n=5): Mean age 38.1 years (SD 9.5) Ongoing IONP (n=7): Mean age 34.8 years (SD 4.9) CON (n=7): Mean age 36.9 years (SD 8.7)	To investigate pain sensitivity between acute and ongoing IONP compared with CON.	No intervention.	Supraorbital (SO) Infraorbital (IO) Mental foramen, mandibular (MM) Median nerve, cubital fossa (ME) Ulnar nerve, medial epicondyle (UL) Radial nerve, intermuscular septum at triceps (RA) Articular pillars of C5/C6 (Cx)	No side differences were found. Lower PPTs were observed over trigeminal sites (SO & MM) in ongoing but not acute IONP compared to CON. Decreased PPTs were observed for both IONP groups over ME and UL, while only the ongoing IONP group had lower PPTs over RA, compared to CON. Lower PPTs in ongoing but not acute

				2nd metacarpal (2M) Tibialis anterior (TA) (Bilateral: 1-cm^2 probe 30 kPa/s)	IONP over Cx, 2M and TA.
¤§Λ(Johnston et al., 2008a)	IONP grouped by level of disability No disability (IONP1; n=33): Mean age 43 years (SD 10.6) Low disability (IONP2; n=38): Mean age 43.8 years (SD 9.4) Moderate/severe disability (IONP3; n=14): Mean age 45.4 years (SD 10.3)	To investigate the relationship between pain sensitivity and disability in office workers with and without symptoms.	No intervention.	Upper trapezius (UT) Levator scapulae (LS) Semispinalis capitis (SM) Tibialis anterior (TA) Median nerve, cubital fossa (ME) (Bilateral: 1-cm^2 probe 40 kPa/s)	No side difference was found. For the ME and TA, lower PPTs were seen for IONP3 compared to IONP1 and CON.

	CON (n=22): Mean age 37.4 years (SD 10.4)				
*§(Karlsson et al., 2015)	NSP (n=41): Median age 42 years (25th & 75th percentile: 37 & 49) CON (n=24): Median age 41 years (25th & 75th percentile: 28 & 48)	To investigate differences in pain sensitivity, algesic and analgesic substances in response to exercise between an NSP population and CON.	PPT measurements were conducted at baseline and within 5 days after the last exercise session. Exercise program 3x/week for 4-6 months: Strengthening exercises using dumbbells or a stretching program.	Trapezius muscle (a mean value of 3 points was used for analysis): T1 (medial) T2 (middle) T3 (lateral) Tibialis anterior (TA) (Bilateral, but only data from the most painful side for NSP and the dominant side for CON were reported: 1-cm^2 probe 40 kPa/s)	At baseline the NSP group had significantly lower PPTs for both the trapezius muscle and TA compared to CON. The NSP group displayed significantly increased PPTs at the trapezius muscle following the exercise intervention.
*¤§Λ(Kasch et al., 2001)	Acute WAD (n=40): Mean age 35.6 years (SD 10.7)	A prospective study investigating sensitization following acute WAD injury.	PPTs were recorded at baseline and follow-up sessions conducted at 1-week, 1-month, 3- & 6-months (Only data from day 0 and day	Upper trapezius (UT) Masseter (MS) Temporalis (TM)	At baseline the WAD group had lower PPTs compared to CON for all sites except for UT and LP. At day 90 only the LP site was non-significant.

	CON (ankle injury; n=40): Mean age 34.8 years (SD 12)		90 is presented in the article).	Sternocleidomastoid (SCM) Infraspinatus (IS) Left proximal interphalangeal joint (LP) (Bilaterally for all but the LP site, but unclear if the reported results are a mean of the two sides: 1-cm^2 probe 33 kPa/s)	At 6 month follow-up there were no group differences.
*¤(Koelbaek Johansen et al., 1999)	WAD grade II-III (n=11): Mean age 42 years (Range 28-69) CON (n=11): Mean age 39 years (Range 26-50)	To investigate the presence of increased sensitivity following experimental pain in a WAD population compared to CON.	PPTs were only obtained prior to the experimental session (hypertonic saline (5.8%) infused in the anterior tibial muscle).	Infraspinatus (IS) Brachioradialis (BR) Tibialis anterior (TA) (Most affected side for WAD: 1-cm^2 probe 30 kPa/s)	At baseline the WAD group had significantly lower PPTs at all sites compared to CON.

*(La Touche et al., 2010)	IONP (n=23): Mean age 28 years (SD 5) CON (n=23): Mean age 28 years (SD 6)	To investigate the presence of trigeminal sensitization in IONP compared to CON.	No intervention.	C5/C6 zygapophyseal joint (C5/C6) Temporalis (TM) Masseter (MS) Upper trapezius (UT) Tibialis anterior (TA) (Bilateral: 1-cm^2 probe)	No side differences were found. IONP had significantly lower PPTs at all sites except the TA compared to CON.
*¤§#(Larsson et al., 2008)	TM (n=20): Mean age 43.8 years (SD 9.8) CON (n=20): Mean age 45.2 years (SD 11.3)	To investigate alterations in nociceptive substances in the upper trapezius muscle during daily work between TM and CON.	PPT was recorded at a clinical examination prior to the test day (8hr work day).	Upper trapezius (UT) Middle trapezius (MT) Lower trapezius (LT) Tibialis anterior (TA) (Bilateral: 1-cm^2 probe 30kPa/s)	TM had significantly lower PPTs for UT compared to CON for the most painful side but not for the contralateral side. No difference was observed for the TA.

¤(Lopez-de-Uralde-Villanueva et al., 2016)	IONP (n=54): Mean age 44.56 years (SD 14.44) IONP with neuropathic features (IONP NF; n=53): Mean age 43.27 years (SD 14.47) CON (n=53): Mean age 44.25 years (SD 12.43)	To investigate potential differences in PPT and cervical range of motion in IONP, IONP NF and CON.	No intervention.	Sub-occipital muscles (SO) Upper trapezius (UT) Lateral epicondyle (LE) Tibialis anterior (TA) (Bilaterally for all, but no side differences were found so the mean was used for analysis.: 1-cm^2 probe)	Both neck pain groups displayed reduced PPTs at SO and UT. Only the IONP NF group had lower PPTs at LE and TA, which were significantly reduced compared to both IONP and CON.
§(Ng et al., 2014)	WAD Grade II (n=30): Mean age 44.3 years (SD 9.6) CON (n=30): Mean age 44.1 years (SD 10.2)	To investigate cervical range of movement and the somatosensory profile of WAD compared to CON.	No intervention.	Mid cervical spine at C5 level (C5) Median nerve trunk at the elbow (MN) Tibialis anterior (TA) (Bilateral for all but C5, no side differences were found so the mean was used for	The WAD group displayed reduced PPTs at all sites compared to the CON group.

				analysis: 1-cm^2 probe 40kPa/s)	
^(Schomacher et al., 2013)	NP (n=10): Mean age 34.1 years (SD 8.8) CON (n=9): Mean age 27.2 years (SD 4.1)	To investigate neck muscle activity during head movements as well as determining PPT at the neck in NP and CON.	PPT recordings were conducted prior to a series of circulatory neck movements with 15N and 30N pressure. Each movement series lasted 12-s and was separated by 2-min rest.	C2/C3 zygapophyseal joint (C2/C3) C5/C6 zygapophyseal joint (C5/C6) (Most painful side: 1-cm^2 probe 30kPa/s)	NP displayed lower PPTs at both sites compared to CON. For both groups lower PPTs were observed at C2/C3 compared to C5/C6.
(Scott et al., 2005)	IONP (n=20): Mean age 32 years (SD 11) WAD (n=30): Mean age 41.6 years (SD 10) CON (n=20): Mean age 31.25 years (SD 10)	To investigate sensory changes in WAD and IONP compared to CON.	No intervention.	C2/C3 zygapophyseal joint (C2/C3) C5/C6 zygapophyseal joint (C5/C6) Median nerve trunk (MN) Ulnar nerve trunk (UN) Radial nerve trunk (RN)	WAD: Reduced PPTs at all sites except UN when compared to CON. IONP: Lower at C2/C3 and C5/C6 but not at any other site when compared to CON. WAD only differed from IONP by a

				Tibialis anterior (TA) (Bilateral for all, no side differences were found so the mean was used for analysis: 1-cm^2 probe 40kPa/s)	significantly lower PPT at C5/C6.
*¤§#Λ(Sjors et al., 2011)	TM (n=19): Mean age: 40 years (Range 28-48) CON (n=30): Mean age: 40 years (Range 26-50)	To investigate the presence of increased sensitivity in regard to PPTs and the response to experimental pain in TM compared to CON.	PPTs were only obtained prior to the experimental session (hypertonic saline (5.8%) injected in the right anterior tibial muscle).	Trapezius muscle (a mean value of 3 points was used for analysis): T1 (medial) T2 (middle) T3 (lateral) Tibialis anterior (TA) (Bilateral: 1-cm^2 probe 40 kPa/s)	At baseline the TM group had significantly lower PPTs bilaterally over the trapezius muscle and the TA compared to CON.
(Smith et al., 2017)	WAD grade II (n=21): Mean age 44.5 years (SD 10.5) CON (n=19): Mean age 37.4 years (SD 10.8)	To compare the effect of isometric and aerobic exercises on pain sensitivity in WAD compared to	2 exercise tasks separated by 5-10days. 1) 30-min submaximal cycling exercise	Mid cervical spine at C5 level (C5) Tibialis anterior (TA) (Unclear if TA was measured bilaterally: 1-cm^2 probe 40 kPa/s)	WAD had reduced PPTs at both sites at baseline compared to CON. CON had higher power output during exercise 1 and did

		CON.	2) Isometric wall squat with knees bent at 100° until fatigue (max 3-min).		exercise 2 for a longer duration than WAD. Both groups displayed significantly increased PPTs at all sites following exercise 2 but not exercise 1.
§¤(Sterling et al., 2003)	WAD grade II-III (n=80): Mean age 36.27 years (SD 12.69) NDI score at 6 months was used make 3 WAD subgroups: WAD1: Recovered WAD2: Mild symptoms WAD3: Moderate/severe symptoms	Prospective study to investigate potential differences in pain sensitivity between those who recover and those who develop ongoing symptoms following whiplash injury.	No intervention. WAD were assessed at 1, 2, 3 and 6 months post injury while CON was assessed 3 times separated by 1 month.	C2/C3 zygapophyseal joint (C2/C3) C5/C6 zygapophyseal joint (C5/C6) Median nerve trunk (MN) Ulnar nerve trunk (UN) Radial nerve trunk (RN) Tibialis anterior (TA) (Bilateral, but unclear if the reported results are a mean of the two	WAD3 displayed reduced PPTs at all sites when compared to both CON and WAD1&2. WAD3 did not show any changes in PPTs throughout the study. WAD1&2 had lower PPTs at C2/C3 and C5/C6 compared to CON at baseline but this was not significantly different after 2 months.

	CON (n=20): Mean age 40.1 years (SD 13.6)			sides: 1-cm^2 probe 40kPa/s)	
§¤(Sterling et al., 2004)	Acute WAD grade II-III (n=80): Mean age 33.5 years (SD 14.7) Cluster analysis of NDI score was used to make 3 WAD subgroups: WAD1: Mild symptoms WAD2: Moderate symptoms WAD3: Severe symptoms CON (n=20): Mean age 39.5 years (SD 14.6)	To investigate cervical range of motion and motor control along with the sensory profile of acute WAD.	No intervention.	C2/C3 zygapophyseal joint (C2/C3) C5/C6 zygapophyseal joint (C5/C6) Median nerve trunk (MN) Ulnar nerve trunk (UN) Radial nerve trunk (RN) Tibialis anterior (TA) (Bilaterally for all, no side differences were found so the mean was used for analysis: 1-cm^2 probe 40kPa/s)	WAD1 was not significantly different from CON. WAD2&3 displayed reduced PPTs at all sites except UN when compared to CON.

¤Λ(Sterling et al., 2002)	WAD grade II-III (n=115): Mean age 36.83 years (SD 10.9) CON (n=95): Mean age 38.95 years (SD 14.47)	To investigate PPTs in ongoing WAD.	No intervention.	C1/C1 zygapophyseal joint (C1/C2) C2/C3 zygapophyseal joint (C2/C3) C5/C6 zygapophyseal joint (C5/C6) Greater occipital nerve (GN) Median nerve trunk (MN) Ulnar nerve trunk (UN) Radial nerve trunk (RN) Tibialis anterior (TA) (Bilateral: 1-cm^2 probe 40kPa/s)	No side differences were found. Significantly reduced PPTs were seen for the WAD group compared to the CON group at all sites.

(Uthaikhup et al., 2015)	IONP (n=30): Mean age 62.2 years (SD 3.7) CON (n=30): Mean age 70.6 years (SD 3.4)	To investigate pain sensitivity in elders with IONP.	No intervention.	C5/C6 zygapophyseal joint (C5/C6) Tibialis anterior (TA) (Bilateral, but no side difference was found and the mean was used analysis: 1-cm^2 probe 40kPa/s)	The IONP group displayed significantly lower PPTs at C5/C6 but not at TA compared to CON.
¤(Van Oosterwijck et al., 2012)	WAD grade I-III (n=22): Mean age 38.4 years (SD 9.2) CON (n=22): Mean age 37.1 years (SD 14.6)	To examine the effects of exercise with different intensities on pain inhibition in WAD and CON.	2 bike exercise tasks separated by 1 week. 1) Submaximal exercise. 2) Self-paced exercise.	Web between thumb and index finger (TI) Low back lateral to L3 (L3) Calf muscle (CM) (Bilateral, but unclear if the reported results are a mean of the two sides: 1-cm^2 probe 1-kg/s)	At baseline WAD had a lower PPT at CM compared to CON. Following exercise 1, CON had increased PPTs at all sites, while WAD had decreased PPT at all sites, causing these to be significantly different between groups. After exercise 2, PPT at CM had increased for WAD and this was no longer different from CON, while PPTs were still decreased at

					all other sites.
¤(Wallin et al., 2012)	WAD grade II-III (n=28): Mean age 40.1 years (SD 7.1) CON (n=29): Mean age 35.4 years (SD 10.6)	To investigate potential differences in the somatosensory profile of WAD compared to CON.	No intervention.	Average of three points over the Upper trapezius (UT) Tibialis anterior (TA) (Bilateral: 1-cm^2 probe 30kPa/s)	WAD had lower bilateral PTTs at all sites compared to CON.

Appendix B. A summary of studies investigating AM in clinical neck pain during upper limb activity

Appendix B. A summary of studies examining effect of clinical neck pain on axioscapular muscle function, using electromyography (RMS EMG; recorded using surface electrodes if nothing else is mentioned), compared to healthy controls: * Including neck AND shoulder pain; € Including altered scapula position; ¤ Including arm symptoms; # Participants diagnosed with trapezius myalgia; ^ Patient group not clearly defined; § Studies including neck pain of less than 3months duration AND/OR without daily symptoms. Only EMG parameters from the neck, shoulder and axioscapular muscles are reported. Studies with no control groups have been excluded. Whiplash associated disorders (WAD), Insidious onset of neck pain (IONP), Neck pain (NP = mix of different types), Neck and shoulder pain (NSP), Trapezius myalgia (TM), Healthy controls (CON).

Reference	Study population:	Aim of study	Task investigated	Muscles investigated (side)	Main findings
§#(Andersen et al., 2008)	TM (n=42): Mean age 44 years (SD 8) CON (n=20): Mean age 45 years (SD 9)	To investigate the effect of TM on axioscapular muscle function during dynamic and static arm exercises.	Scaption/shoulder abduction (15° to the fontal plane): Slow and fast concentric contractions, slow eccentric and static contractions.	Upper trapezius (UT) Medial deltoid (MD) (Monitored side was not clear)	TM displayed decreased activity for UT during all but fast concentric contraction while no difference was observed for the non-painful MD when compared to CON.

*§(Andersen et al., 2014)	TM (n=42): Mean age 44 years (SD 8) CON (n=20): Mean age 45 years (SD 9)	To compare muscle activity during fatigue and the effect of different rehabilitation interventions for a TM population compared with CON.	100 consecutive cycles of shoulder elevations (2-s maximal voluntary contractions) followed by 2-s rest. Measurements pre- & post a 10 week training program (1 hr/week): SST: Specific strength neck/shoulder exercises GFT: General fitness training on exercise bike REF: Group counselling with regard to workplace ergonomics.	Upper trapezius (UT) (UT was monitored on the most painful or dominant side)	At baseline peak UT activity was lower in TM than CON but there was no difference in resting activity. No significant changes were found following the intervention.
€§(Castelein et al., 2016)	IONP (n=19): Mean age 28.3 years (SD 10.1),	To investigate axioscapular muscle activity and the influence of scapula	Two exercises in the scapular plane, 30° to frontal plane: 1)	Upper trapezius (UT) Middle trapezius (MT)	In participants with scapula dyskinesia, reduced MT activity was seen in IONP

	CON (n=19): Mean age 29.3 years (SD 11.7)	dyskinesia during arm elevation in IONP and CON.	Scaption 2) Sliding a towel up a wall. Both exercises consisted of a 4-s elevation and 4-s lowering phase.	Lower trapezius (LT) Serratus anterior (SA) Intramuscular EMG: Pectoralis minor (PM) Levator scapula (LS) Rhomboids (RM) (Muscles were monitored on the dominant side)	compared to CON during scaption. During towel slide IONP had higher PM activity than CON.
^*¤(Elcadi et al., 2013)	NSP (n=18): Mean age 43.44 years (SD 10.60) CON (n=17): Mean age 39 years (SD 12.11)	To investigate differences between CON and participants with work-related neck/shoulder and/or forearm pain.	5-s maximal voluntary isometric contraction (MVIC) in shoulder elevation from a seated neutral position, followed by isometric contraction intensities of 10%, 30%, 50% and 70% of MVIC for 20s. 2-min rest between	Upper trapezius (UT) (UT was monitored on the right side)	No difference between the NSP group and CON for the UT.

			each contraction.		
*(Falla et al., 2004a)	IONP (n=10): Mean age 33.6 years (SD 9.8), WAD (n=10): Mean age 32.4 years (SD 7.6) CON (n=10): Mean age 31.4 years (SD 11.5)	To investigate if a low load functional task causes alterations in muscle activity for IONP and WAD compared to CON.	Moving a pen between 3 circles at 88 beats/min for 2-min with the right arm.	Upper trapezius (UT) Sternocleidomastoid (SCM) Anterior scalene (AS) (Muscles were monitored bilaterally)	WAD showed higher bilateral activity for SCM and AS during the entire task when compared to CON. Furthermore a bilateral increased activity of UT, SCM and right AS post task was seen for WAD when compared to CON. WAD showed greater bilateral activity for AS and SCM during and post task while right UT activity was only increased during the post measurement when compared to IONP. IONP showed greater bilateral SCM activity during the task while this was only true

					during part of the task for the left AS when compared to CON. A reduced activity was seen for the right UT for IONP compared to CON during the task. Additionally increased activity was seen in the post measurement for the left SCM when comparing IONP to CON.
§#(Goudy and McLean, 2006)	TM (n=24): Mean age 39.8 years (SD 8.4) CON (n=27): Mean age 45 years (SD 8.3)	To develop a myoelectric model to discriminate between TM and CON.	4-s static contraction in 90°scaption. Static contraction in 45° for as long as possible (max 30min.).	Upper trapezius (UT) (Ipsilateral UT was monitored)	No significant group difference was found in muscle activity for the two tasks, but TM had increased activity in the rest period following the 45° contraction task compared to CON.
(Helgadottir et al., 2011)	IONP (n=22): Mean age 35 years (SD 8)	To compare axioscapular muscle activity in IONP and CON	Slow scaption movements performed in a seated position.	Serratus anterior (SA) Upper trapezius (UT)	IONP & WAD showed significantly delayed onset and reduced duration of

	WAD (n=27): Mean age 33 years (SD 10) CON (n=23): Mean age 30 years (SD 8)	during arm movements.		Middle trapezius (MT) Lower trapezius (LT) (Ipsilateral muscles were monitored)	muscle activity for SA compared to CON.
¤§Λ(Johnston et al., 2008c)	Office workers with IONP grouped by level of disability (NDI) No disability (IONP1; n=33): Mean age 43.2 years (SD 10.6) Mild disability (IONP2; n=38): Mean age 43.8 years (SD 9.2) Moderate disability (IONP3; n=22):	To assess cervical range of motion, muscle activity and motor control in office workers with IONP (with or without arm pain) and CON.	From a comfortable sitting position participants moved a pen between 3 circles with their dominant arm, at 88 beats/min for 5-min.	Upper trapezius (UT) Anterior scalene (AS) Sternocleidomastoid (SCM) Cervical erector spinae (CES). (Muscles were monitored on the dominant side)	CES along with the UT, SCM and AS displayed higher activity in IONP2&3 compared to CON during the task. Additionally the UT & CES was more active post exercise in IONP 2&3 compared to CON. No difference in muscle activity was observed between IONP 1-3.

	Mean age 33.5 years (SD 3.6) CON (n=22): Mean age 37.3 years (SD 10.4)				
¤§∧(Johnston et al., 2008b)	Office workers with IONP grouped by level of disability (NDI) No disability (IONP1; n=33): Mean age 43 years (SD 10.6) Mild disability (IONP2; n=38): Mean age 43.8 years (SD 9.4) Moderate/severe disability (IONP3; n=14):	To measure work stressors and muscle activity in female office workers with IONP (with/without arm pain) and CON.	3 tasks of 5-min each, separated by a few minutes of rest: 1) A standard typing task 2) A standard typing task but with emphasis on fast and accurate typing 3) A Stroop color word test where participants had to call out the color of the print (forearms resting on the desk).	Upper trapezius (UT) Anterior scalene (AS) Sternocleidomastoid (SCM) Cervical portion of Erector spinae (CES). (Muscles were monitored bilaterally)	Workers in general displayed higher bilateral muscle activity than CON except for UT. IONP1 differed from IONP3 by displaying greater activity for the right CES. In general IONP2&3 had higher activity for UT and CES than CON during post measurements, while this was only true for UT when compared to IONP1.

	Mean age 45.4 years (SD 10.3) CON (n=22): Mean age 37.4 years (SD 10.4)				
#§∧(Larsson et al., 2000)	TM (n=25): Mean age 47 years (SD 10) CON1 (n=25): Mean age 46 years (SD 11) CON2 (n=21): Mean age 48 years (SD 6)	To investigate the relationship between occupation (TM & CON1 = Cleaners; CON2 = Teachers), myalgia and performance.	From a seated position participants performed dynamic maximal shoulder flexion followed by a passive extension using the dominant arm.	Upper trapezius (UT) Anterior deltoid (AD) Infraspinatus (IS) Biceps brachii (BB) (Ipsilateral muscles were monitored)	No significant differences were observed for TM compared to CON1. TM showed higher activity for UT and IS during the passive extension of the shoulder when compared to CON2.
*¤§#(Larsson et al., 2008)	TM (n=20): Mean age 43.8 years (SD 9.8) CON (n=20): Mean age 45.2 years (SD 11.3)	To investigate alterations in nociceptive substances in the upper trapezius muscle between TM and CON	Investigated parameters were recorded during an 8hr workday.	Upper trapezius (UT) (UT was monitored on the dominant side)	No significant difference was found between groups.

		during daily work.			
*¤#∧(Larsson et al., 1999)	TM (n=76): Mean age 42 years (Range 23-58) CON (n=20): Mean age 44 years (Range 25-63)	To investigate the presence of local physiological changes in TM compared to CON.	Periods with different static workload: 1) Bilateral scaption to 30°, 60°, 90° & 135° for 1-min, separated by 1-min rest. 2) Condition 1 repeated with 1kg (Women) or 2kg (Men) load in each hand. 3) Fatigue task at 45° holding 1kg (Women) or 2kg (Men).	Upper trapezius (UT) (Muscles were monitored bilaterally)	TM had a tendency toward higher activity on the most painful side during both loaded and unloaded activity when compared to CON although this was not significant.
*§(Leonard et al., 2010)	NSP (n=25): Mean age 20.7 years (SD 2) CON (n=25): Mean age 21.0 years (SD 1.5)	To investigate muscle activity for the upper trapezius between symptomatic and asymptomatic students during a functional task.	From a comfortable seated position participants performed a 30-min writing task.	Upper trapezius (UT) (Ipsilateral UT was monitored)	Significantly higher muscle activity was observed for the UT in the NSP group compared to CON.

*§(Madeleine et al., 1999)	NSP (n=12): Mean age 47.4 years (SEM 1.84) CON (n=6): Mean age 43.8 years (SEM 2.75)	To investigate the effects of NSP on muscle activity during a standardized low load task compared to CON.	A 3-min repetitive cutting task using a knife (resembling an industrial work task).	Upper trapezius (UT) Anterior deltoid (AD) Middle deltoid (MD) Infraspinatus (IS) (Muscles were monitored on the right side)	No significant differences were found in RMS EMG between groups.
*§(Nederhand et al., 2002)	WAD (n=19): Mean age 39.1 years (SD 12.9) IONP (n=18): Mean age 47.1 years (SD 12.2) CON (n=18): Mean age 38.9 years (SD 12.4)	To investigate potential differences in patterns of muscle activation between IONP and WAD and CON.	From a comfortable sitting position participants moved a pen between 3 circles with their dominant arm, at 88 beats/min for 2-min.	Upper trapezius (UT) (Muscles were monitored bilaterally)	No significant group differences were found during exercise, but WAD had a tendency toward increased activity post exercise compared to CON or IONP which was more obvious on the dominant side compared to the non-dominant side.

*¤§∧(Nilsen et al., 2006)	NSP (n=29): Mean age 41.1 years (SD 11.3) CON (n=35): Mean age 39.7 years (SD 12.2)	To investigate muscle activity at rest and during a 60-min low-grade stressful functional task in NSP and CON.	5-min rest period followed by a 60-min stressful reaction time task where one of two keys had to be pushed on a keyboard. The stressful task was followed by a 30-min rest period.	Upper trapezius (UT) Temporal (TP) Frontal (FT) Splenius (SP) (Muscles were monitored bilaterally)	No significant group difference was seen.
*¤§#(Schulte et al., 2006)	TM (n=7): Mean age 49.4 years (Range 45-47) CON (n=9): Mean age 49.9 years (Range 43-60)	To investigate differences in muscle activity between TM and CON.	From a seated position participants performed a 6-min isometric shoulder elevation task (dominant arm) against a force transducer at 30% of maximal voluntary contraction.	Upper trapezius (UT) Biceps brachii (BB) (Muscles were monitored on the dominant side)	Lower muscle activity in both UT and BB was seen for TM compared to CON.
*¤§#(Sjogaard et al., 2010)	TM (n=43): Mean age 43.8 years (SD 9.8)	To investigate potential metabolic changes for the upper trapezius during a work	Participants performed a 40-min unilateral pegboard (repositioning a stick 30-cm) task followed by 20-min rest before a 10-min stressful	Upper trapezius (UT) (Ipsilateral muscles were monitored)	TM displayed higher UT activity during both tasks compared to CON.

	CON (n=19): Mean age 45.2 years (SD 11.3)	task in TM and CON.	STROOP test using a computer mouse.		
*¤§#(Sjors et al., 2009)	TM (n=18): Mean age 40.0 years (SD 6.0) CON (n=30): Mean age 39.9.2 years (SD 5.6)	To investigate if participants with TM display different physiological responses to a repetitive and a stressful task compared to CON.	20-min rest before 3x 20-min functional tasks: 1) Simulated assembly line 2) Fine finger dexterity 3) Pegboard exercise. This was followed by The Trier Social Stress Test, then an 80-min rest period.	Upper trapezius (UT) Deltoid muscle (DM): Unclear which part of the muscle is investigated. (Ipsilateral muscles were monitored)	TM had higher activity during rest and functional tasks compared to CON, while no significant difference was seen during the stressful task.
*¤§(Szeto et al., 2005)	NSP (n=23): Mean age 36.0 years (SD 4.6) CON (n=20): Mean age 31.3 years (SD 7.2)	To investigate muscle activity in symptomatic and asymptomatic office workers during a prolonged computer task.	Participants were seated at a standard office workstation with keyboard and chair self-adjusted for comfort. Participants performed a standardized 1-hour typing task at their own pace.	Upper trapezius (UT) Lower trapezius (LT) Anterior deltoid (AD), Cervical erector spinae (CES)	Right CES was more active in CON than NSP, while right UT was more active in NSP than CON. Muscle activity in the low discomfort group resembled controls more than it

				(Muscles were monitored bilaterally)	resembled the high discomfort group.
*¤§Λ(Szeto et al., 2009)	NSP (n=21): Mean age 28.0 years (SD 9.0) CON (n=18): Mean age 24.0 years (SD 2.0)	To investigate if office workers with NSP endure higher muscle loads during typing tasks when compared to CON and if this is similar for different tasks.	From a seated position participants performed 3x 20-min computer tasks separated by a 5-min rest period: 1) Typing/ copying a text 2) Muse task (playing minesweeper) 3) first type a word from a list and then copy/paste the word using the mouse.	Upper trapezius (UT) Cervical erector spinae (CES) (Muscles were monitored bilaterally)	For the mouse task, increased activity of the left UT was seen in NSP compared to CON. CES had higher activity in all tasks bilaterally for NSP than CON, except the left side during the mouse task.
*§(Takala and Viikari-Juntura, 1991)	NSP (n=10): Mean age 36.5 years (SD 3.4) CON (n=10): Mean age 36.6 years (SD 3.1)	To investigate bilateral muscle activity in symptomatic and asymptomatic workers during a static upper limb task.	From a seated position participants were asked to move a pen every 5-s between 9 holes on a plate put in front of them.	Upper trapezius (UT) Thoracic erector spinae (TES) (Muscles were monitored bilaterally)	No significant group differences.

§(Tsang et al., 2014)	IONP (n=30) Mean age: 38.3 years (SD 11.35) CON (n=30): Mean age 35.1 years (SD 9.0)	To investigate cervical and thoracic movement and muscle recruitment patterns during a functional task in IONP and CON.	From a seated position participants were asked to, with the right arm, lift a 2kg weight from a desk in front of them to a shelf 70-cm above. The weight was released before they had to pick it up and return it to the desk again.	Cervical erector spinae (CES). Sternocleidomastoid (SCM) Upper trapezius (UT) Thoracic erector spinae – T4 level (TES4) & T9 (TES9) (Muscles were monitored bilaterally)	The IONP group had lower acceleration and velocity in cervical flexion and extension movements during the task compared to CON. While raising the arm, the IONP group displayed longer duration of muscle activity for UT bilaterally, left CES, left SCM, bilateral TES4 and right TES9 compared to CON, while this was only true for right TES4 in the release phase. When lowering the arm, the IONP displayed longer duration of muscle activity for right UT, bilateral SCM and right TES4.

*§(Voerman et al., 2007)	NSP (n=21): Mean age 31.0 years (SD 7.6) WAD (n=20): Mean age 31.8 years (SD 8.6) CON (n=20): Mean age 33.6 years (SD 5.5)	To demonstrate that NSP and WAD show comparable muscle activity which is different from CON.	2 computer tasks of 10-min each: 1) Typing task 2) Modified Stroop task (stressful) involving mouse clicks. Before each typing task a 2-min rest period was used, and a rest period of 5-min was used post each task.	Upper trapezius (UT) (UT was monitored bilaterally)	No significant differences were observed between groups during the two tasks.
€§(Wegner et al., 2010)	IONP (n=18) with altered scapular position: Mean age 27.2 years (SD 6.9) CON (n=20): Mean age 24.8 years (SD 6.6)	To investigate differences in muscle activity during a functional task between CON and IONP patients with altered scapular position, and to determine if this is affected by postural correction.	From a comfortable seated position participants performed a 5-min typing task. The IONP group then got 5-10-min of individualized postural correction training before repeating the typing task.	Upper trapezius (UT) Middle trapezius (MT) Lower trapezius (LT) (Muscles were monitored on the painful side)	The IONP group displayed increased activity of MT and decreased activity of LT when compared to CON, which was not the case after the postural correction.

*(Xie et al., 2016)	NSP (n=20): Mean age 24.6 years (SD 3.1) CON (n=20): Mean age 23.2 years (SD 3.1)	To investigate muscle activity during mobile texting and computer typing in NSP participants and CON.	3 standardized typing tasks: 1) Texting on a mobile phone using both thumbs 2) Texting on a mobile phone using the right thumb 3) Typing on a computer using both hands.	Upper trapezius (UT) Lower trapezius (LT) Cervical erector spinae (CES) Extensor carpi radialis (ECR) Extensor digitorum (ED) Flexor digitorum superficialis (FDS) Abductor pollicis brevis (APB) (Muscles were monitored on the right side)	NSP displayed a tendency for higher UT activity during both typing and texting tasks when compared to CON.
€(Zakharova-Luneva et al., 2012)	IONP (n=18): Mean age 27.4 Years (SD 7.0)	To identify differences between IONP displaying altered scapular	Isometric shoulder abduction, external rotation and flexion.	Upper trapezius (UT) Middle trapezius (MT)	Increased activity in LT during abduction and external rotation but not in flexion when comparing IONP to CON. No

	CON (n=20): Mean age 24.9 Years (SD 6.7)	orientation and CON.		Lower trapezius (LT) (Muscles were monitored on the most painful side for IONP while the side was random for CON)	alterations for UT or MT were observed.

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